RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES
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ADMINISTRATION OF ARTIFICIAL PNEUMOTHORAX UNDER FLUOROSCOPIC GUIDANCE

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THE following presentation is a preliminary report of special artificial pneumothorax work being carried out for the past several months at Temple University Hospital, namely, the administration of artificial pneumothorax under direct fluoroscopic guidance. For many years large numbers of pneumothorax cases have been receiving refills in this hospital, with the development of a large pneumothorax clinic. Such a clinic is absolutely essential for the follow-up treatment of patients discharged from hospitals and sanatoria. The routine procedure in the artificial pneumothorax clinic has been to fluoroscope the patient in the upright position immediately before the treatment. The fluoroscopic examination includes a direct fluoroscopic tracing of the entire chest, with particular reference to the shape and position of the collapsed lung. The patient is then sent to the operating room, placed in the usual pneumothorax position, lying on the "good" side, and given four or five hundred cubic centimeters of nitrogen in the usual way. Encountering difficulty in the administration of gas to a formerly easy case whose fluoroscopic tracing showed a well collapsed lung suggested to one of us (J. B.) the possibility of giving the treatment directly under fluoroscopic guidance. This treatment was successfully performed with the aid of the fluoroscope without the slightest difficulty. Since then a regular special clinic has been held every week for the treatment of difficult cases under fluoroscopic guidance, with gratifying results. This clinic has proven of inestimable value to us, and failure to find any reference to this type of work in the literature has prompted us to describe our procedure.

After the first few refills were performed by the fluoroscopic method it became clear to us that the universally routine method of fluoroscopic control of pneumothorax cases suffers frequently from a very glaring error. The usual method employed in most clinics is to fluoroscope the patient in the upright position just before the treatment and then to administer the gas with the patient lying on a stretcher. Often a marked change in the fluoroscopic appearance of the collapsed lung occurs when the patient is changed from the upright position to the lateral decubitus pneumothorax position. To determine just what does happen we have routinely fluoroscoped all our patients in the upright and in their exact pneumothorax position with the horizontal ray, and have found very definite differences which will be described in the accompanying diagrams. It is very easy to understand why occasional difficulty in giving a refill occurs when one has accurate evidence of the difference in the two fluoroscopic tracings of the same case. It required merely a fluoroscopic study of a few cases with the horizontal ray to

demonstrate to us that this method is indispensable. It gives us a much more accurate picture of the position and shape of so easy and simple as to cause us to feel that pneumothorax treatment in a particular case should never have to be discon-

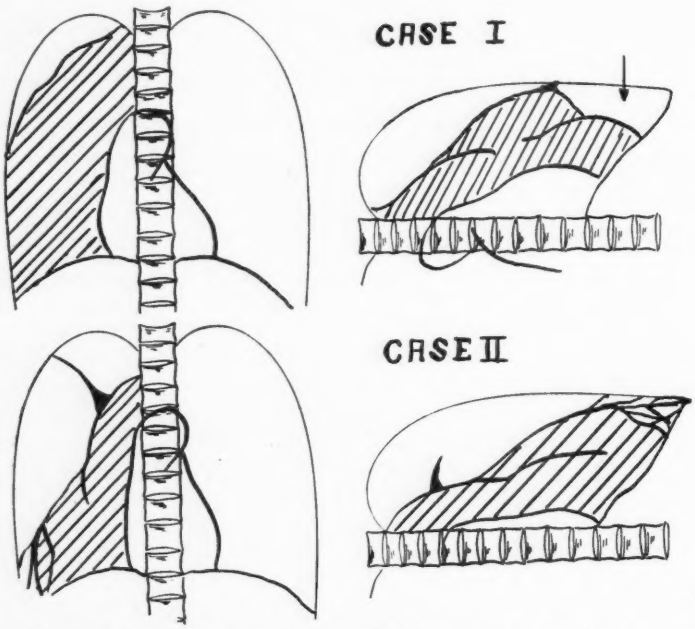

Fig. 1. Case I. The diagram in the upright position is a ventral projection and shows an apical collapse. The lateral decubitus position, dorsal projection, reveals a partial collapse of all portions of the right lung, except that part prevented from collapsing by an adhesion. Blood-spitting frequently followed administration of treatment through the usual axillary site. Under fluoroscopic guidance the pneumothorax needle was introduced at the position indicated by the arrow and the refill treatment was successfully given without any blood-spitting sequelæ.

Case II. The tracing made in the upright position is a ventral projection, while the horizontal is a dorsal projection. The network of adhesions at the costophrenic angle prevents a greater collapse and may be the cause of difficulty in administering the refill treatment, if the needle is introduced at the right costophrenic angle.

the collapsed lung at the time of the treatment, thus minimizing difficulty and, in some cases, danger of lung injury.

Fluoroscopic pneumothorax administration, we believe, is indicated in any case in which the operator has difficulty in doing a refill. The treatment is given with ease and accuracy and the fluoroscopist can indicate to the operator the exact interspace to use, can watch the needle enter the pleural cavity, and see the lung collapse as though he were looking directly into the pleural cavity. There is no harm to the patient and the technic is tinued solely because of difficulty of administration of the gas. In the comparatively short time during which we have been availing ourselves of this additional help in pneumothorax technic, it has already given us a feeling of assurance about difficult cases which we never had before. Now we know that when a patient in the regular clinic gives us trouble, the treatment can usually be continued without difficulty under fluoroscopic guidance. This method may also later prove to be helpful in initial cases and in trying to find loculated fluid in the pleural cavity for

diagnostic aspiration. Of course, it goes without saying that fluoroscopic pneumothorax technic is not a routine procedure.

In the upright position the patient is studied in the antero-posterior, postero-anterior, lateral, and oblique positions,

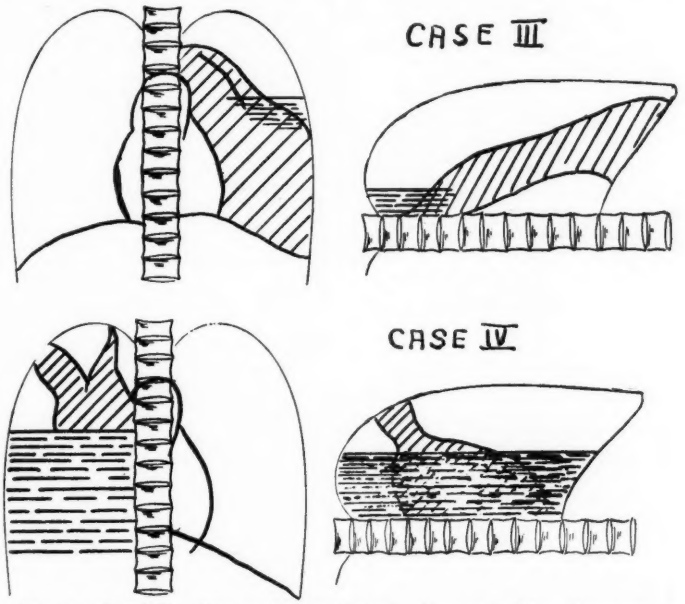

Fig. 2. Case III. The upright and the horizontal position diagrams are ventral projections. The examination in the upright position reveals a selective apical collapse with fluid overlying the expanded portion of the lung. The position of the fluid suggests that the expanded lung is adherent to the thoracic wall and that partial obliteration of the pneumothorax has occurred. The lateral decubitus position (ventral projection), however, reveals a good collapse and the lung is found not to be adherent to the thoracic cage. Note the shifting of the fluid.

Case IV. The upright diagram is a ventral projection, while the lateral decubitus is a dorsal projection. Note the size of the pneumothorax and the collapse of the lung on change of position.

The vast majority of pneumothorax cases present no difficulty in treatment, but there are always present, in large clinics, a few cases which worry the operator and an occasional case that has to be discontinued because the operator cannot find the pleural cavity. In just such cases we believe that fluoroscopic guidance is indispensable.

TECHNIC

No special equipment is necessary to carry out this work. The ordinary upright fluoroscope and the biplane are equally adaptable to carry out this procedure. We have made use of both.

the most suitable one being determined for each patient individually. A direct tracing of the chest and the relative positions of the heart, trachea, hilar regions, diaphragm, and position and shape of the collapsed lung is made. Then the patient lies on a stretcher on the unaffected side with a pillow under the axilla and the affected side of the chest is fluoroscoped, using the horizontal ray. Again the findings are traced directly on a 14 × 17 inch celluloid transparency. The transparencies are placed on the screen and the tracing is made with a black china marking pencil (No. 163 T Blaisdell).

In our experience a hooded surgical table is most suitable since it can be continually

illuminated with a red light, thus providing sufficient illumination for preparing the skin and for the operator to observe the

A consideration of vital importance is the exposure of the operator's unprotected hand to the primary beam. We have made

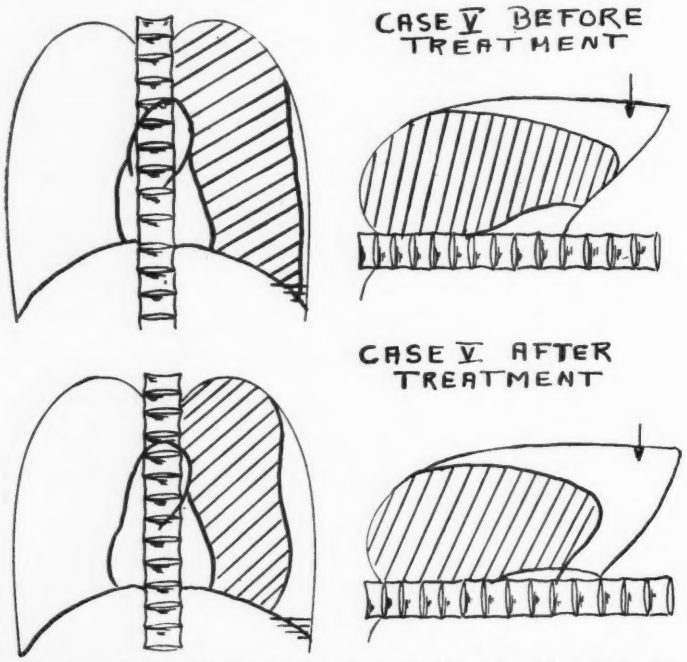

Fig. 3. Case V. Diagrams of the chest showing the position of the left lung before and after treatment. The upright and horizontal position diagrams are ventral projections. Arrow indicates position of pneumothorax needle during treatment.

manometric oscillations and the amount of fluid in the bottles without interfering with fluoroscopic visualization. Our present source of light is a small portable flashlight fitted with a red filter.

The most suitable place for the insertion of the needle is located fluoroscopically. The skin is prepared with iodine and two applications of alcohol and the patient is draped. Local anesthesia is employed in every case. Under fluoroscopic guidance the needle is introduced into the pleural space and its position is always carefully observed, especially in those cases in which the needle is introduced at the costophrenic angle or into a very small pneumothorax pocket. While the air is being injected into the pleural cavity the collapse of the lung and change in the position of the lung, diaphragm, heart, and mediastinum are carefully observed.

it a practice to use as small an aperture as possible and to keep the operator's hand out of the beam at all costs. With this in mind we have devised a lead shield which is readily attached to the operator's arm and always offers adequate protection to the hand in case it may be exposed momentarily to the primary beam.

REPORT OF CASES

The following selected cases illustrate a few common differences between the fluoroscopic tracings made with the patient in the upright position and in lateral decubitus. In these cases the fluoroscopic pneumothorax technic proved to be of great value.

Case I, E. T. Examination of the chest with the patient upright revealed a minimal collapse of the right apex. With the

patient on his side, on the other hand, an adhesion which prevented the mid-portion of the lung from collapsing was demonstrated. Above and below this adhesion, however, a fairly large pneumothorax was apparent. On several occasions treatments administered through the usual axillary site caused blood-spitting. Since then the treatments have been successfully given at the costophrenic angle (at position of arrow, ninth interspace) with fluoroscopic guidance.

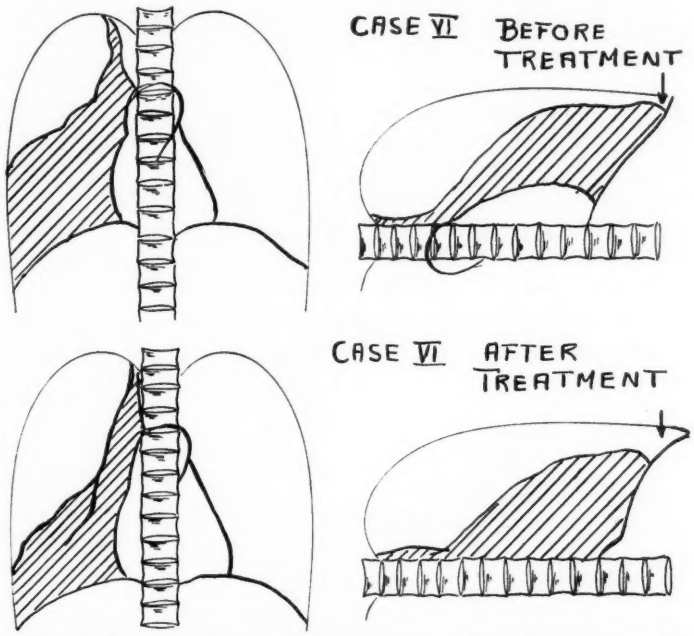

Fig. 4. Case VI. The two upright diagrams are ventral projections and the other two are dorsal projections. Because on several occasions difficulty was encountered in finding a pneumothorax pocket, fluoroscopic guidance was used and enabled us to find a very small pocket of air at the costophrenic angle into which the needle could be safely introduced. Note change in position of lung when patient is studied in the lateral decubitus position.

Case II, L. E. This case demonstrates lower lobe adhesions. No appreciable change was noted in the appearance of the collapsed lung when the patient lay on the unaffected side; the adhesions prevented a greater collapse. Inserting the pneumothorax needle in this region might lead to difficulty in administering the treatment.

Case III, P. A. The upright roentgenogram and fluoroscopic diagram reveal an apical collapse, with a small amount of fluid overlying the lung, which appears to be adherent to the thoracic cage. This appearance is suggestive of an obliterative pneumothorax. Fluoroscopic study with the patient in the lateral decubitus position showed the lung to be well collapsed and not adherent to the chest wall. In this position the fluid shifted to the mediastinal aspect of the left apex.

Case IV, D. C. A case of hydropneumothorax showing the importance of studying the patient while he is lying on the unaffected side. The shifting of the fluid reveals a large pneumothorax and a good collapse of the lung.

Case V, J. B., 21 years of age. The lung is adherent at the left apex. At the left base the lung is sufficiently collapsed to visualize a small pneumothorax pocket; this is better demonstrated when the patient is examined in lateral decubitus. Un-

der fluoroscopic guidance the pneumothorax needle was introduced at the costophrenic angle and a successful collapse of the lung was obtained without encountering any difficulty whatever.

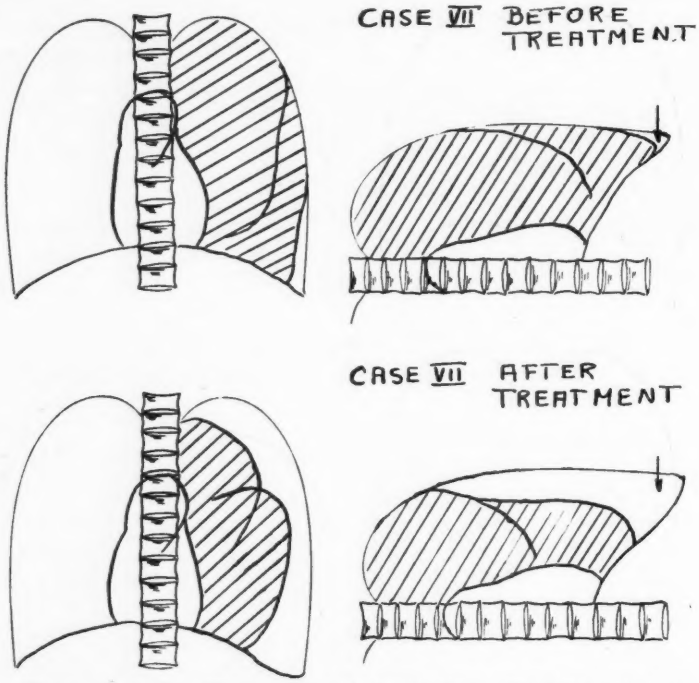

Fig. 5. Case VII. These are all ventral projections. The left lung is practically entirely expanded except for the small pneumothorax pocket at the left costophrenic angle. Under fluoroscopic guidance the pneumothorax needle was safely introduced into this space and a very satisfactory collapse was obtained, as is shown by the two lower diagrams.

Case VI, I. G. The upper two diagrams show the appearance of the right chest before treatment. Because of difficulty in the administration of the treatment in the right axilla, the pneumothorax needle was inserted at the costophrenic angle, even though the pneumothorax space was minimal. The position of the needle was carefully watched and at no time was there any danger of injury either to the lung or to the diaphragm.

The lower two diagrams show the resulting pneumothorax.

Case VII, E. M. This patient, as in Case 6, illustrates the costophrenic pocket of gas into which the pneumothorax needle was easily introduced under fluoroscopic guidance.

Altogether, we have studied 80 pneumothorax patients for comparative data on the position of the thoracic viscera in the upright and in the lateral decubitus positions. To date, we have given 40 pneumothorax treatments under fluoroscopic guidance to 20 individual pneumothorax patients. We have attempted the administration of initial pneumothoraces with this procedure but as yet a sufficient number have not been performed to properly evaluate its usefulness.

SUMMARY

We have studied 80 individual pneumothorax cases to determine the difference in the appearance of the chest in the upright and in the lateral decubitus positions. The

fluoroscopic examination of the patient in the lateral decubitus position is essential for a better understanding of the actual difficulties that one may encounter when giving a pneumothorax refill and for localization of the most suitable space for the insertion of the pneumothorax needle. This has led us to the following conclusions:

1. The fluoroscopic and roentgenographic appearances which have led to the characterization "selective pneumothorax" are often completely absent when the patient assumes a horizontal position. Present-day conceptions of so-called "selective pneumothorax" must be modified.

2. Any case which presents difficulty during administration of the refill should have the advantage of fluoroscopic guidance before further treatment is discontinued. All guess-work in the difficult cases has been replaced by direct observation and accurate guidance. The feeling of relief and assurance which has come to us through this procedure is hard to express on the written page.

3. The carrying out of the pneumothorax treatment under fluoroscopic guidance should be reserved for difficult cases only. In these cases it is an indispensable adjunct to our armamentarium in collapse therapy.

Further observations that may follow a larger experience with this work will be reported at a later date.

HISTOGENESIS OF BASAL-CELL EPITHELIOMA[1]

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I WISH to discuss the histogenesis of benign and malignant forms of basal-cell epithelioma of the skin proper, admitting the fallacy of attempting to solve the pathogenesis of a given tumor from study of the morphologic changes only. The observation of many types of epithelioma in various stages of development, compared with the clinical findings and subsequent course of the type of neoplasm in question, permits, I believe, the drawing of conclusions regarding their histogenesis. I favor Krompecher's concept of the basal-cell origin of these tumors, but I shall attempt, nevertheless, to clarify divergent points of view as expressed recently by Haythorne, who supports Mallory's (46 and 47) concept of a hair-matrix origin for *Basalzellenkrebse* (Krompecher), and by Glasunow, who expressed the belief in their benign and dysontogenetic nature, and would call these tumors "facial fissure cancroids" or "haut carcinoid."

Confusion has arisen, I believe, through failure to distinguish between the benign and malignant forms of basal-cell epitheliomas, to study lesions in their earliest stages, and to prove by serial section or various methods of reconstruction their origin primarily from hair follicle, sweat gland, or sebaceous gland. The term "epithelioma" includes both benign and malignant cutaneous neoplasms, because a sharp distinction between the two is not always possible (36). The term "carcinoma" is restricted to rare cases of adenocarcinomas of sweat glands and sebaceous glands, and to metastatic lesions in the skin from carcinoma elsewhere in the body. Although I have read well over a thousand articles on epithelioma, I shall refer only to the more recent and pertinent literature. The reader is also referred to various chapters in Jadassohn's Handbuch (2, 8, 27, 54, and 73), especially, and to the new editions of Ormsby's and Sutton's textbooks on dermatology and those on dermatohistopathology by Freiboes, Gans, and McCarthy.

To simplify the discussion, a working classification of basal-cell epithelioma is given, recognizing the fact that the so-called epithelial nevi (referring especially to verruca senilis), nevus pigmentosus, and melano-epithelioma may not properly belong in this group, and that transitions between benign and malignant forms of epithelioma frequently occur. I shall discuss histopathologic changes and embryologic and etiologic factors in the various subgroups.

CLASSIFICATION OF EPITHELIOMA PRESUMABLY OF BASAL-CELL ORIGIN

I. *Benign.*—
- (*A*) Epithelioma adenoides cysticum (Brooke), including tricho-epithelioma (Jarish) and adenoma sebaceum (Pringle).
- (*B*) Cylindroma (nevus epithelioma cylindromatosis—Gans, endothelioma capitis—Spiegler).
- (*C*) Syringoma (syringocystadenoma).
- (*D*) Epithelial nevi (Jadassohn and Gans).
  1. Verruca senilis, including dermatosis papulosa nigra.
  2. Sweat gland and sebaceous gland nevi of various types.
- (*E*) Nevus pigmentosus.

II. *Malignant.*—
- (*A*) Basal-cell epithelioma (Krompecher's *Basalzellenkrebs*).
  1. Superficial epitheliomatosis (erythematoid benign epithelioma—Little).
- (*B*) Basal-squamous-cell epithelioma.
- (*C*) Melano-epithelioma arising from basal or dendritic cells or both, including melanotic whitlow and so-called lentigo maligna.

[1] Submitted for publication, April 23, 1935.

III. "*Precancerous Dermatoses.*"—

(*A*) Xeroderma pigmentosum (frequently).

(*B*) Senile keratoses and keratoses which are the sequelæ of radiotherapy, arsenic, and tar (occasionally). Basal-cell epithelioma never develops in true cases of Bowen's and Paget's diseases.

HISTOLOGY AND EMBRYOLOGY

The complexity and divergent views regarding the embryology of the epidermis and cutis, the status of the so-called basement membrane, and the relationship between elastic tissue, connective tissue, and *Gitterfasern* is reviewed by Lynch (43) and also Pinkus (68). The hair follicle results from an invagination of the epidermis, and the outer root sheath of the follicle is composed of basal cells, as is also the outer layer of the sweat ducts and sebaceous glands. My observations, which support Peck's views that both basal and dendritic cells are melanoblasts and that dendritic cells are probably modified basal cells, admit that the question of pigment-formation is not yet settled (51). Pigment-containing cells are normally seen in the outer root sheath only to the depth of the rete ridges, although the cells of the hair matrix and bulb give a positive dopa reaction (67). In my experience, the basal cells of the epidermis have prickles or intercellular bridges comparable to the prickle-cell layer. I likewise am in accord with the views of Broders (10) and Hansemann regarding the anaplasia and dedifferentiation of individual cells. A basal tumor cell that retains its ability to form pigment is more differentiated and, therefore, less malignant than a basal tumor cell which multiplies without the formation of pigment. Only the basal cells and a varying number of layers of prickle cells above them are potentially neoplastic, as cells that have undergone even partial keratinization are no longer capable of reproduction.

This study is based on twelve years' clinical and histopathologic observations of cutaneous neoplasms. The tissue for the most part has been fixed in formalin or absolute alcohol and stained routinely with hematoxylin and eosin, van Gieson's stain, elastin H, or Unna's acid orcein and polychrome methylene blue for elastic fibers, and in many cases with silver nitrate stain for melanin and Maersch's modification of the Bielschowsky stain for *Gitterfasern*. In some cases Unna's neutral orcein, Masson's trichrome stain, and similar connective tissue stains, various silver stains for nerve fibers, and frozen sections for "dopa" were studied.

BENIGN FORMS OF BASAL-CELL EPITHELIOMA

Epithelioma Adenoides Cysticum, Syringoma, and Cylindroma.—The typical cases of epithelioma adenoides cysticum, syringoma, and cylindroma may be differentiated clinically by their different size and situation of the lesions (76). The first may have a hereditary basis; the others apparently have not. In many cases, however, clinical and histologic features of two or more of these conditions are seen in the same individual (36, 53 and 82) or even in the same specimen for biopsy (35, 75 and 80). Whereas, cylindroma is usually confined to the scalp (71), I have seen several cases in which a solitary lesion occurred on an arm or leg, which histologically presented the rather characteristic hyaline changes within and about the nests of tumor cells. None of these conditions clinically suggest a malignant process.

Ingels' patient (Fig. 1-*A*), whom I was able to observe clinically and pathologically for a period of years, presented both clinical and histopathologic features of epithelioma adenoides cysticum, syringoma, and adenoma sebaceum (Pringle). The case was also unusual clinically in that lesions first appeared when the patient was 36 years of age, rather than in childhood. The generalized distribution and small size of the individual lesions, together with the involvement of the dorsum of the phalangeal joints, suggested the clinical diagnosis of pityriasis rubra pilaris. Wax recon-

struction of serial sections from a portion of the nevoid plaque on the back, and of a lesion on the dorsum of the hand, revealed that the origin of the epithelial strands and cysts was not only from the hair-matrix cells and basal cells of the outer root sheath of the hair follicle, but also from the basal cells of the epidermis and the more superficial portions of the sweat ducts (Fig. 1-*B*).

Fig. 1. Epithelioma adenoides cysticum with features of syringoma (Ingels). (*A*) Multiple points of origin of epithelial strands and cysts from epidermis, hair follicle, and atypical sweat ducts with comma-like tail: (*B*) wax reconstruction of serial sections, showing interrelation between epidermis, cysts, ducts, and hair follicles (the bulbous areas represent cysts of various origin).

After further observation of the patient at the meeting of the Chicago Dermatological Society, in October, 1934 (Arch. Dermat. and Syph., May, 1935, **31**, 738), which included specimens for biopsy of the early lesions on the trunk and thigh, I am convinced that the changes start intra-epidermally, some of the cell nests, strands, and cysts developing into rudimentary hair follicles and others into strands which resemble sweat ducts; occasionally, an epithelial strand showed abortive attempts to form sebaceous cells. It was impossible to trace a direct connection of the sweat-duct-like

strands to normal sweat glands, probably because the cells of the sweat glands, *per se*, are too differentiated as a rule to give rise or to revert to a basal-cell tumor. Definite connection with normal sweat glands has not been proved in any case of epithelioma adenoides cysticum. Weidman (83) emphasized that one cannot classify precisely each benign cutaneous epithelioma either as a tumor or sweat duct or hair follicle, or as a tumor of the superficial epidermis, because all three can be derived from a common embryonal structure, namely, the skin plate of Remak, which is at first not a sweat duct, epidermis, or hair follicle. If the skin plate has fully differentiated, then one sees, as in Stillians' case, a sweat gland in one place, a hair follicle in another, and a Krompecher epithelioma in another. Kyrle (39) would attribute syringoma to aberrant apocrine glands, a view which I have been unable to substantiate in seven cases which I have studied.

I wish to point out that even true metaplasia may occur in the cells of the epidermis that have begun to differentiate toward sweat ducts. This was evidenced in a case, reported by Walther and myself, in which metaplasia toward mucinous glands was seen in a verrucous lesion of the palm of the hand, and where such glands normally do not occur.

It becomes evident that even in the case of epithelioma adenoides cysticum (tricho-epithelioma), origin is not solely from the walls or matrix cells of a hair follicle. All these tumors may be regarded as benign basal-cell growths, although some cases of syringoma (82) and cylindroma may be regarded as harmatoma in the sense of Albrecht, *i.e.*, a tumor which is formed from misplaced embryonic cells. I do not believe that any of these tumors are potentially malignant except that any epithelial proliferation, when subjected to trauma, irritation, or inadequate removal, may undergo malignant change.

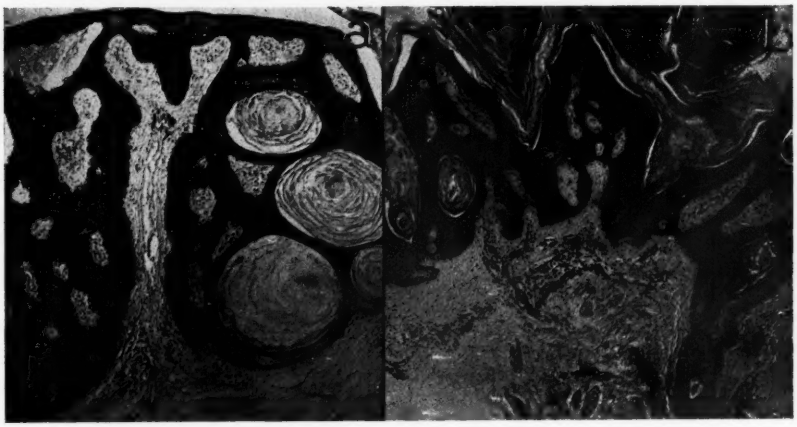

Fig. 2. (*A*) Verruca senilis of forehead. Solid type with cysts, and strands simulating tricho-epithelioma. Marked deposit of melanin pigment in basal cells; also some in chromatophores in cutis; (*B*) verruca senilis near ear—verrucous type. Note acanthosis and hyperkeratosis, as well as pigmented basal cells and apparent involvement of hair follicle (silver nitrate and hematoxylin).

Verruca Senilis.—Verruca senilis has been designated by Becker as a basal-cell growth. He apparently regarded as unimportant the definite phenomena of keratinization and cornified cysts, which are present, and which as a rule do not connect with either hair follicles or sebaceous glands. Freudenthal, Freudenthal and Spitzer, and I (58) have emphasized the occasional histologic resemblance of verruca senilis to tricho-epithelioma; in certain areas the growth may be chiefly basal-cell in character, and the formation of pigment usually

is marked. Prickle cells are also present in these strands of epithelial cells (Fig. 2-*A*). In the verrucous and hyperkeratotic forms of the disease (58), and in contradistinction to Becker's statements (4), definite acanthosis (hyperplasia of prickle cells) is very obvious, as may be seen in Figure 2-*B*. In all forms of verruca senilis, the cysts represent invagination of the epidermis, and are composed of stratum corneum; this is the result of a relatively normal and regular cycle of keratinization (34). Because of this, I would prefer to group verruca senilis with delayed epithelial nevi. Several authors, Eller and Anderson, and Becker (5), have referred to benign not nevoid melanoepithelioma of Bloch (7) and have ignored the fact that Bloch's cases were submitted for publication simultaneously with those of Freudenthal, and probably without knowledge of Freudenthal's concept of differentiation of verruca senilis and keratoma senile. Judging from Bloch's description and illustrations, both Dörffel and I (17) believe that Bloch's first case fulfills the histologic requirements of a pigmented intra-epidermal epithelioma of Jadassohn, with both basal-cell and squamous-cell growths *in situ;* whereas, his second case fulfills all the requirements of a verruca senilis, as does Becker's Figure 21 of his Case 7, in a recent article in the *American Journal of Cancer* (3), and also Figure 47 of Eller and Anderson, and probably Haythorne's Figures 18 and 19. It is this pedunculated elevated type of verruca senilis which may be confused clinically with a verrucous pigmented nevus, and which, because of the excessive pigment formation that gives it a black appearance, may be considered a true melanoma, and therefore be excised. Occasional instances in which verruca senilis has undergone malignant change, usually basal-cell in character, have been reported (17 and 69). Eller and Ryan reported a questionable case of a basal-cell epithelioma on a seborrheic keratosis. I believe that photomicrographs of this case (Figs. 10 to 13 in their report) show a typical picture of the solid type of verruca senilis, with benign proliferation of basal cells. I have seen a few cases of verruca senilis which have shown basal-cell or even squamous-cell malignant change, but only as the result of repeated trauma and irritation, or inadequate removal. I agree with Freudenthal that verruca senilis is a benign process which rarely reveals either clinical or pathologic evidence of malignant change.

Nevus Pigmentosus.—If one accepts Peck's opinion that both basal cells and dendritic cells of the epidermis are true melanoblasts, then one has support for Unna's concept of the epithelial origin of pigmented nevi. Becker (6) has recently summarized the concept that pigmented nevi are Schwannoma, on the basis of Masson's concept (48, 49, and 50) of the neurogenic character of moles. Laidlaw pointed out the necessity of comparing the pigmented nevi of human beings to amphibian or reptilian tactile spots to explain the complex and confusing picture of moles which affect human beings. I have seen a fair percentage of nevi in which the so-called "lames foliaces," which resembled tactile corpuscles, were present. Masson's "celles claires" appear to be modified dendritic cells. From experience in studying *Gitterfasern* (lattice fibers or reticulum) in various dermatoses, and as a result of an intensive study of a case of ganglioneuroma (60), I believe that it often is very difficult to distinguish terminal nerve fibrils from connective tissue and *Gitterfasern,* by differential staining only. Broders and Fletcher have commented on Masson's views, and have said: "It seems reasonable to assume that since the nervous system and the epidermis develop from the ectoderm, and since moles are of epidermal origin, that their spheroidal cells which we believe to be in an undifferentiated or embryonic state are atavistic to the extent that they are capable of differentiating into nervous tissue, and therefore in such a light may be considered of a neuro-epithelial nature."

As a bridge or gap between benign and malignant basal-cell neoplasms of the skin, Nomland's case, which histologically showed malignant basal-cell epithelioma

that clinically resembled benign pigmented basal-cell nevi, is a good example. In this connection, see Figure 3-*A* of a lesion, which had been present for twelve years on the cheek of a man aged 32 years, and which had been diagnosed clinically as a nevus sebaceous. The histopathologic picture at the left is that of a nevus sebaceous. There

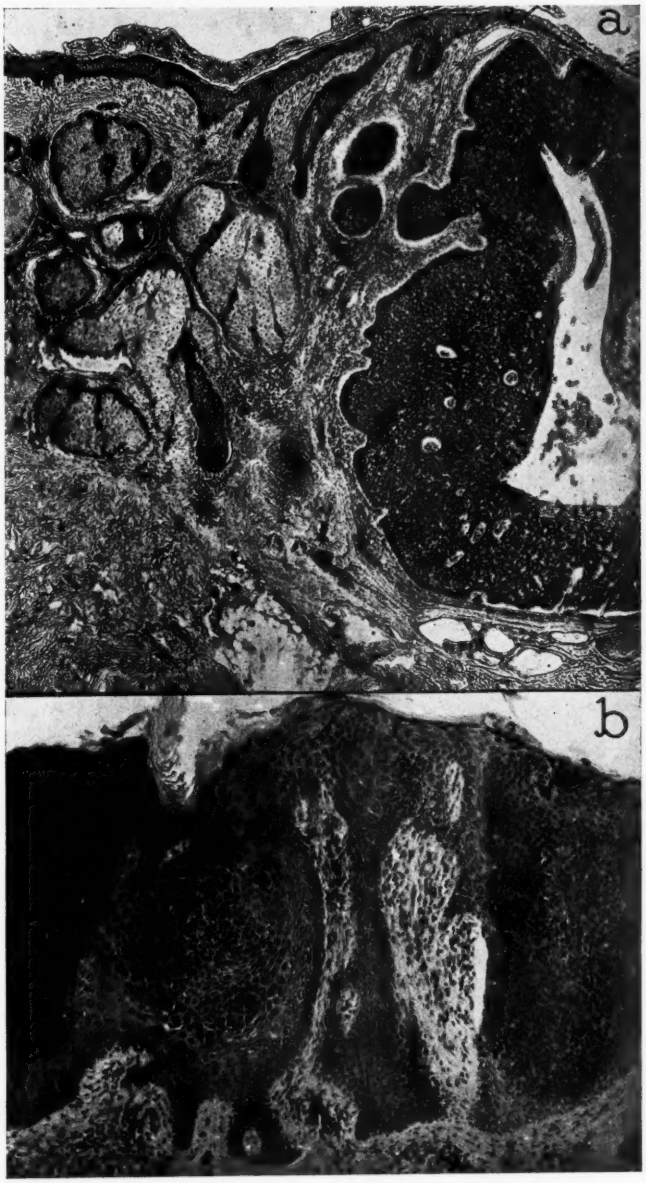

Fig. 3. (*A*) Nevus sebaceus, plus a large basal-cell tumor whose connection with the basal cells of the epidermis could be traced but not to hair follicles, to the dilated sweat glands beneath same, or to the sebaceous nevus; (*B*) intra-epidermal epithelioma (Jadassohn), showing basal-cell epithelioma arising from basal cells of epidermis and growing upward instead of downward; also area of squamous-cell epithelioma *in situ*.

are early proliferative changes in the hair follicles, and at the right there is a tumor mass, which was diagnosed as basal-cell epithelioma, and which was composed of basal cells that could be traced in serial sections to the basal cells of the epidermis but not to either the sebaceous nevus or hair follicle or to the dilated sweat glands lying beneath the tumor mass. The columnar arrangement of the outer layer of cells, the cystic center, and the extravasation of erythrocytes suggested the diagnosis of cylindroma, but without corroborative evidence of hyaline or other changes. (See also cases of Jadassohn (36) and his Figure 5, and Szodoray in which there was a closer relation between nevus sebaceous and basal-cell epithelioma.) The epithelioma which occasionally develops in sebaceous cysts may be basal cell in character (15).

The ability of patients to present multiplicity in types of lesions is also exemplified by Jadassohn's case, in which a patient had psoriasis of the hand, which was treated with roentgen rays. A Bowen-like roentgen epithelioma developed subsequently in one area of the hand, and a low grade squamous-cell epithelioma developed in another area of the same hand. This was associated with an adenoid epithelioma (70), which possibly belonged to the benign sweat gland group. The intra-epidermal epithelioma of Jadassohn (Fig. 3-*B*), which I believe belongs properly to a subdivision of superficial epitheliomatosis, is an example of both basal-cell and squamous-cell growths, which occur in the same lesion but remain *in situ* and, therefore, are relatively benign in nature (13).

MALIGNANT FORMS OF BASAL-CELL EPITHELIOMA

Basalzellenkrebs (Krompecher).—It has been repeatedly confirmed that ordinary basal-cell epithelioma (Krompecher's *Basalzellenkrebs*) has a predilection for certain regions on the face, namely, the forehead, nose, and inner aspects of the cheeks (30 and 61), which also are frequently the sites of the benign epithelioma which was mentioned previously. McDonagh called attention to the fact that many mammals, especially deer, have specialized hairs in the orbital facial fold, and explained basal-cell epithelioma on the basis of the lack of need of things that are present in the lower animals, and on the basis of hereditary cell rests. Glasunow expressed the opinion that basal-cell epithelioma on the face commenced in and about the lines of fusion of the embryonic facial processes. Paljtschewsky emphasized the fact that basal-cell growth appear in areas, which are well supplied with sebaceous glands, and often arise from comedones or nevi. Mallory, speaking of basal-cell epithelioma said: "The cells which arise from a hair matrix and form the hair and its sheath do not differentiate, except to a slight degree, in the way that the cells of the epidermis do. The hair is composed of cells which develop large numbers of delicate fibrils. These fibrils bind the cells closely together. The cells of the sheath on the other hand undergo cornification to a slight extent. . . . Rarely there is a hint of the formation of intercellular bridges and small epithelial pearls are occasionally present." Haythorne believed that special technical methods support the view that so-called basal-cell carcinomas of the skin are really hair-matrix tumors, and that they are associated with changes in the hair follicles and less differentiated portions of the sebaceous glands. The more exact diagnosis would be "hair-matrix carcinomas." He admitted, however, that complete differentiation of hair-matrix tumors and well differentiated hair formation are indeed rare. Kyrle (38) said that the basal-cell layer of the skin has two tasks to fulfill: (1) to differentiate into pavement epithelium, and (2) to act as a matrix for post-fetal formation of sebaceous glands without formation of squamous cells. When tumors, which arise from the basal-cell layer, grow, as in the latter instance, a basal-cell rather than a squamous-cell epithelioma is formed. In connection with Hansemann's theory of anaplasia, Broders (10) said: "Basal-cell epitheliomas control themselves by producing cells simi-

lar to the normal basal cells of the skin." Weidman's concept of various types of tumors, which develop from the embryonic skin plate, has been mentioned previously. Fischer-Wasels has recently presented evidence correlating the Conheim hypothesis of embryonic development with Virchow's irritation theory of the cause of epithelioma.

With the multiplicity of etiologic factors which have been cited previously, it is no wonder that there is still controversy regarding the origin of basal-cell epithelioma, especially of the face, which is the most common situation for this lesion. If the tumor is large and there is apparently a connection with the epidermis, one cannot be sure, from morphologic studies, whether the tumor has originated in the basal-cell layer or is merely a secondary union of an embryonic rest. Thus all combinations of various lesions may be seen, and one sees the ability of basal-cell growths to imitate sweat glands, sebaceous glands, or even hair follicles, without demonstrable proof, in serial sections or wax reconstruction, or origin from any of them. Kyrle justly emphasizes the fact that benign basal-cell growths which may arise from hair follicles (epithelioma adenoides cysticum, trichoepithelioma), are not to be confused with basal-cell carcinoma. The basal cells of the former are smaller in size, more fully differentiated, and show fewer mitotic figures than those of basal-cell epithelioma (carcinoma). I cannot agree with Haythorne, who, on the basis of tinctorial changes and differences in size and character of the cell, regards the junction of basal-cell tumors with the epidermis as false union, as he illustrates, for instance, in Figure 3 of his article. One of the features of malignant basal-cell epithelioma is its propensity for basophilic staining, and the larger and more imperfect forms of individual tumor cells, as compared with normal basal cells, which still retain many of the features of the basal cells of the epidermis, and often the ability to form pigment. The fact that a great many basal-cell epitheliomas are pigmented does not indicate hair-matrix origin any more than it indicates origin from the epidermis, because melanoblasts of both basal and dendritic cells are to be found in both situations. The outlining of basal-cell tumors (81) by a band of *Gitterfasern* (lattice fibers), denies, I believe, the importance of affinity for silver stains as supporting a hair-matrix origin. My experience confirms that of Way, regarding the value of the Maersch-Bielschowsky stain in differentiation of basal-cell, squamous-cell, and melanotic neoplasms by the arrangement of the lattice fibers. Haythorne refers to the longitudinal fibers, which were described by Mallory, as possibly identical with Herxheimer's spirals; the latter were seen both in the epidermis and hair follicle (45).

It has been my experience that the greatest majority of basal-cell epitheliomas of the face show multiple points of origin from the basal cells of the epidermis.

Basal-squamous-cell Epithelioma.—Of considerable significance regarding the basal cell origin of epithelioma, I believe, is the fact which first was brought out most clearly by Darier and Ferrand, and later by myself (55), and by Juon, and by many others, that transitions between basal-cell and squamous-cell epithelioma occur, although Lacassagne, in a comprehensive clinical and pathologic study of 1,075 cases of epithelioma, denied the transition between basal-cell and squamous-cell epithelioma. He failed to refer to any of the articles mentioned previously. From 15 to 20 per cent of the basal-cell epitheliomas which are diagnosed clinically should prove on microscopic examination to be basal-squamous or squamous-cell epithelioma.[2] Basal-squamous-cell epithelioma represents, in the majority of instances, I believe, a true metamorphosis of basal-cell to squamous-cell epithelioma. Partial pearl formation, which characterizes many of these lesions, is composed of basal, intermediary, and prickle cells, resulting in incomplete keratinization, together with a

[2] Epstein, in a study of epithelioma of the skin of the nose, found 96 basal-cell epitheliomas, four squamous-cell epitheliomas, and 15 basal-squamous-cell epitheliomas (metatypical), though only 39 of the 96 basal-cell epitheliomas were proved histologically.

brightly staining colloidal center. The intermediary type of Darier lacks the partial pearl formation, and is composed chiefly of

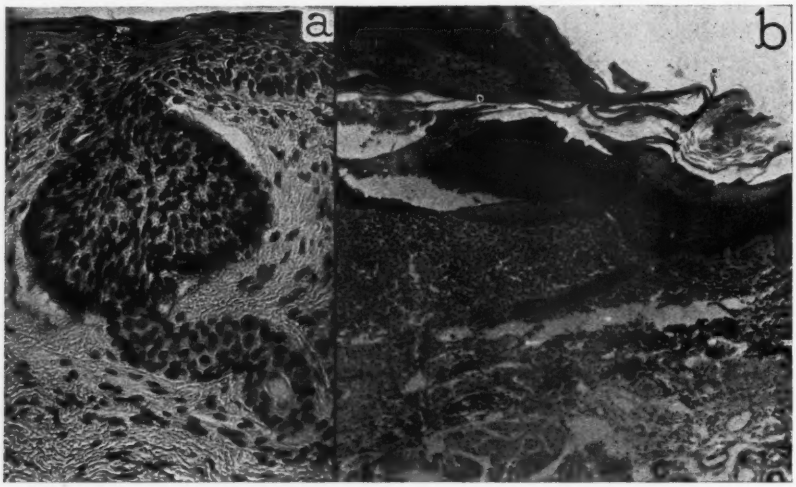

Fig. 4. (*A*) Superficial epitheliomatosis, back. Serial section and reconstruction revealed a basal-cell origin for this tumor, which surrounded the sweat duct but left the latter uninvolved; (*B*) typical lesion of superficial epitheliomatosis, back, of two years' duration, showing ulceration. Multiple points of origin from the basal cells of the epidermis at the left and right. Note the abrupt change and dense basophilic staining of the basal cells, which at the right side are surrounding a sweat duct which remains uninvolved.

cells which are intermediary in character between basal and prickle cells. In Haythorne's article, Figure 4, I believe, does not show a true hair follicle, but shows a parakeratin pearl of early basal-squamous-cell epithelioma. This is definitely different, I believe, from the benign, well-formed cysts, which are seen in verruca senilis, and from the rudimentary or completely developed hair shafts to be seen in various forms of epithelioma adenoides cysticum.

Neither the metatypical nor the intermediary form of basal-squamous-cell epithelioma should be confused with squamous-cell epithelioma Grade 3 or 4, or with those squamous-cell epitheliomas which disclose phenomena of keratinization of individual cells and clumping of cells, and changes that simulate Bowen's disease. From Juon's description and especially Figure 5 of his article of 1933, it seems that his case was not one of pure epithelioma metatypique intermediare, but was one of squamous-cell epithelioma with keratinization of individual cells, as evidenced by his description of Bowen-like changes in both the original and metastatic lesions.

Metastatic Basal-cell Epithelioma.—Basal-cell epitheliomas do not, I believe, metastasize as such. Careful search should reveal basal-squamous cell or squamous-cell changes in the original tumor as well as in the metastatic lesion, at the time of metastasis. The description of the pathologic changes, which was given by Niles, would indicate that this was so in his case (62). He reviewed the older literature, but incorrectly included the two cases, which had been reported by Finnerud, as metastatic basal-cell epitheliomas. I had already included these cases with basal-squamous-cell epithelioma because of their transitional character before metastasis occurred. He was correct in referring to Körbl's Case 61 (erroneously labelled Case 6 in my paper, 55). To this I would also add Beadle's case and Janeway's case; all three of these, however, were reported twenty years or more ago. Both Broders and I (11) have yet to see a case of true metastatic basal-cell epithelioma.

Superficial Epitheliomatosis.—I believe,

however, that the group of epitheliomas, which are usually basal-cell in character, and which Ormsby designated as superficial epitheliomatosis (also referred to as erythematoid benign epithelioma of Little and multiple superficial benign epithelioma of the skin by Wise) offer an ideal field for study of their histogenesis. This is because of their predominance on the trunk and covered portions of the body, where they are removed from the influence of the actinic rays and, for the most part, also from trauma, and also because of their relatively benign character, slow growth, and less frequent change to basal-squamous-cell or squamous-cell epithelioma, as compared with ordinary basal-cell epithelioma. Arsenic has been suggested as an etiologic agent for this group, by Anderson, but as I previously have pointed out (57), I believe he has confused cases of the arsenic type of epithelioma of the trunk with those of superficial epitheliomatosis. Franseen and Taylor, I feel, have fallen into the same error, and thus have a much higher incidence of the arsenic type of basal-cell epithelioma among these cases than is justly so. Confusion arises in cases in which both types of lesions affect the same individual. Before deciding that arsenic is the cause

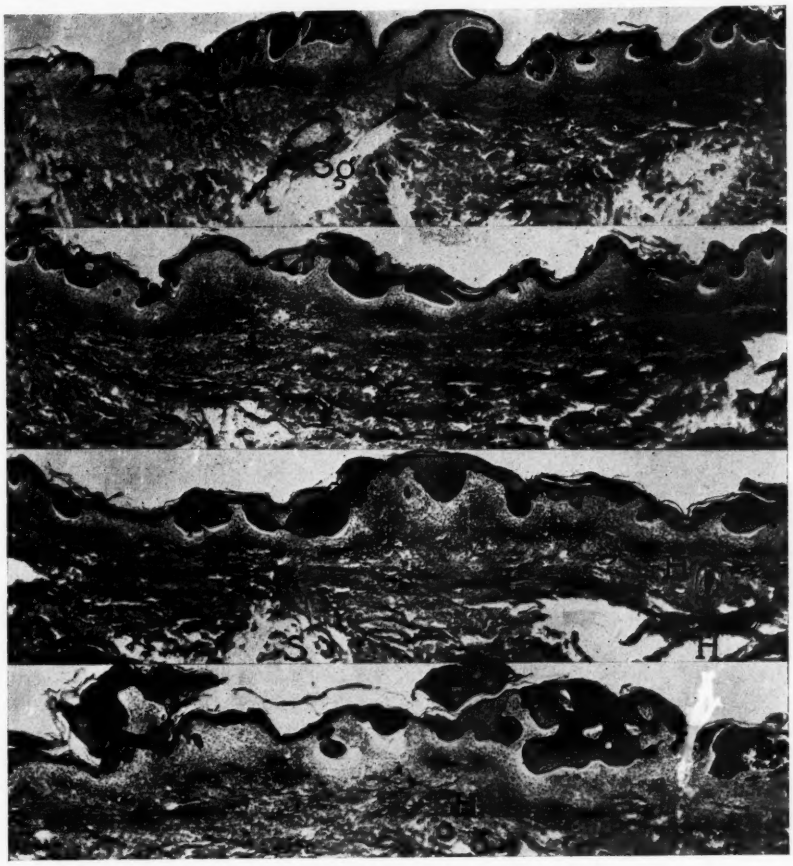

Fig. 5. Typical lesion of superficial epitheliomatosis, right lumbar region, about 2.5 cm. in diameter, from a woman, aged 52 years, who had had a lesion for 15 years. Consecutive series across entire width of lesion (right-hand edge duplicated at next lower left-hand edge), showing multiple basal-cell growths from at least twenty points of origin; also mature sebaceous gland (sg), hair follicle (h), and sweat glands (s).

of a basal-cell epithelioma, one should, as a rule, be able to demonstrate more arsenic in the epithelioma than in the adjacent normal tissue, admitting Fischer-Wasels' evidence that the administration of arsenic may produce a constitutional susceptibility to cancer, or accelerate dormant carcinomatous foci.

A typical case of superficial epitheliomatosis of the dry type is usually basal cell in character, and reveals multiple points of origin from the epidermis. The lesions do not extend deeply; in many instances, it is possible to show by serial section that they are not connected with one another or with the hair follicles. I have seen origins from the basal cells of upper portions of the walls of hair follicles in a few instances but not from the hair matrix. It is interesting that, in contrast to benign basal-cell growths, I have been unable to trace true origin from the walls of a sweat duct (Figs. 4-*A* and 4-*B*). Both of these cases revealed multiple and independent origin from the epidermis, but not from the walls of hair follicles. The proponents of the origin from the hair matrix could say that these are rudimentary hairs inasmuch as, in some mammals and occasionally in human beings, one can see sweat ducts which empty into the orifice of the hair follicle rather than in the epidermis. It is even more difficult, however, to assume in Figure 5, where serial sections reveal more than twenty independent basal-cell growths, that these all should represent rudimentary hair follicles, especially as the section is taken from the right scapular region, in which relatively few hairs are normally seen, and well-developed hair follicles and sebaceous glands, which are cut tangentially, can be seen in several areas, as well as well-developed sweat glands. Furthermore, Figure 6-*A*, which is from the same series of sections as Figure 5, reveals two separate basal-cell growths, which arise from the epidermis and not from the normal fully developed hair follicle which is present. No rudimentary hair follicles were seen in these sections, as are seen in epithelioma adenoides cysticum. One would expect transitional forms to be present if the twenty or more basal-cell growths were of hair follicle or hair-matrix origin. The earliest stages of basal-cell epithelioma, as seen in many cases of superficial epitheliomatosis and in cases in which only a few dozen neoplastic cells are present, may simulate embryonic hairs (see illustrations by Pinkus (68), and by Lewis and Stöhr). Both of these growths show basophilic staining, but the basal-cell epitheliomas reveal larger and more immature forms of basal cells and more mitotic figures than the benign type of growths. The basal-cell growth in superficial epitheliomatosis present a definite band of *Gitterfasern* surrounding the growth. Squamous-cell epithelioma may also arise from the walls of hair follicles, as is seen in Figure 6-*B*.

Studies of superficial epitheliomatosis therefore confirm and support the origin of basal-cell epithelioma from the basal cells of the epidermis.

Melano-epithelioma.—If we believe that dendritic cells are modified forms of basal cells, then melano-epithelioma must also be included in the group of malignant basal-cell epitheliomas. Many writers, however, support Masson's neurogenic origin for these lesions (21, 24, and 41). I have seen all gradations between so-called lentigo maligna (74) and melanotic whitlow to melano-epithelioma, arising from flat to verrucous elevated pigmented nevus (14 and 22). Broders (11) and I are in accord, however, with Becker, and believe that when a malignant change occurs it takes place first at the epidermal-cutis junction, and not, as a rule, deep in the nevus tumor. Whereas the greatest majority of so-called non-melanotic melano-epitheliomas will reveal small amounts of melanin in some areas, when stained with silver nitrate instead of with hematoxylin and eosin stains, this does not deny their relative lack of differentiation, and hence, their greater degree of malignancy than melano-epitheliomas. I do not deny the existence of melanoma, which arises independently from the epidermis, such as malignant change in the nevus blau of Jadassohn.

"PRECANCEROUS DERMATOSES"

Of the so-called precancerous dermatoses (9), xeroderma pigmentosum frequently discloses malignant change in the form of basal-cell epithelioma; some of these growths originate in the hair follicles (59), and many show a considerable degree of pigmentation. In xeroderma pigmentosum, basal-cell tumors predominate over basal-squamous-cell tumors, squamous-cell tumors, and even melano-epitheliomas, and occasionally even sarcomas. In xeroderma pigmentosum, hereditary influences and sensitivity to light, especially to certain wave lengths of light (44), are outstanding etiologic factors.

Studies of senile keratosis, and keratoses that are sequelæ of radiotherapy, arsenic, and tar, reveal that in less than 10 per cent of the cases in which epithelioma develops, is the epithelioma basal-cell in character. When epitheliomas develop, they usually present the histologic picture of a squamous-cell epithelioma *in situ*, with individual cell keratinization, and simulate real cases of Bowen's disease, and may (56, 57, and 58) remain *in situ* for many years before invading the tissue and becoming clinically malignant. Figures 7-*A* and 7-*B* are examples of this. In my real cases of Bowen's disease, I have been unable to find morphologic evidence that would support the concept of some authors that this condition originated in the sweat or sebaceous glands (31 and 72). If, as I have found, malignant change develops in about 20 per cent of the cases of arsenic and senile keratoses, the incidence of basal-cell epithelioma in these cases would be less than 2 per cent. This is not much greater than the incidence of carcinoma of the skin, in general, for the age group and the type of skin under consideration.

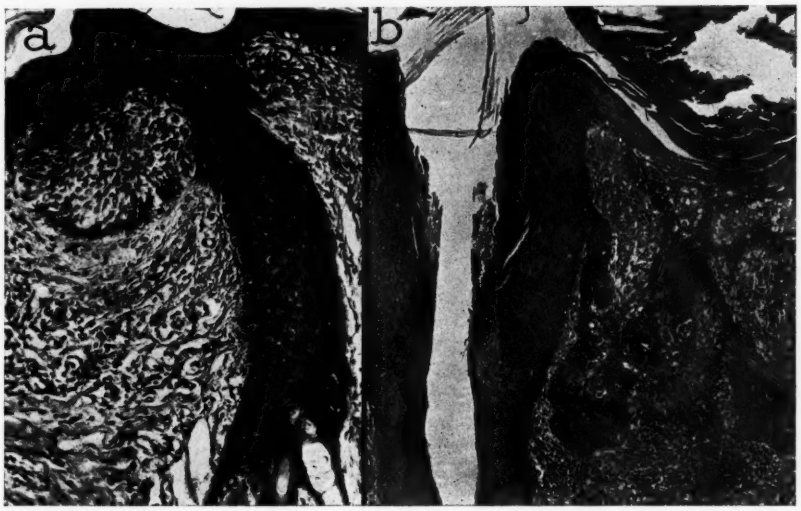

Fig. 6. (*A*) Basal-cell origin about hair follicle without involvement of latter (false hair follicle origin). Same case serial sections as Figure 5; (*B*) squamous-cell epithelioma, Grade 4, cheek, with multiple points of origin from epidermis and wall of hair follicle. (Same case as represented in Figs. 6 and 7, Montgomery and Doerffel.)

SUMMARY AND CONCLUSIONS

Benign forms of basal-cell epithelioma, especially epithelioma adenoides cysticum and cylindroma, may arise from multiple points of origin, from the basal cells of the epidermis, and from the basal cells that form the outer sheath of the hair follicle, sebaceous gland, and sweat duct. At times, they originate from the basal cells of the outer root sheath of the hair follicle, or even from the matrix cells near the bulb, without

evidence that the basal cells of the epidermis participate in the neoplastic process.

Verrucæ senilis may be designated as benign pigmented basal-cell epitheliomas (benign melano-epitheliomas), but I believe they are more properly designated as delayed epithelial nevi. The same holds true for nevus pigmentosus, which should still be classified as a nevus rather than a benign epithelial neoplasm.

Transitions between benign and malignant basal-cell epitheliomas, and multiplicity of type of lesions in the same individual, are seen, and justify the use of the term epithelioma to include both these types of lesions rather than confining epithelioma to benign neoplasms of the skin and carcinoma to malignant forms of same.

The basal cells that line the outer sheath of the hair follicles, sweat ducts, and sebaceous glands are similar to the basal cells of the epidermis, and therefore may participate independently or simultaneously in any neoplastic process.

Malignant basal-cell epitheliomas (Basalzellenkrebs, Krompecher), which predominate in certain locations on the face, may rarely originate from the hair matrix, more often from basal cells of the outer root sheath of the hair follicle, occasionally may represent embryonic rests that are independent of the epidermis or any dermal appendage, but I believe that in the greatest majority of cases they reveal single or multiple points of origin from the basal cells of the epidermis. The latter, in their

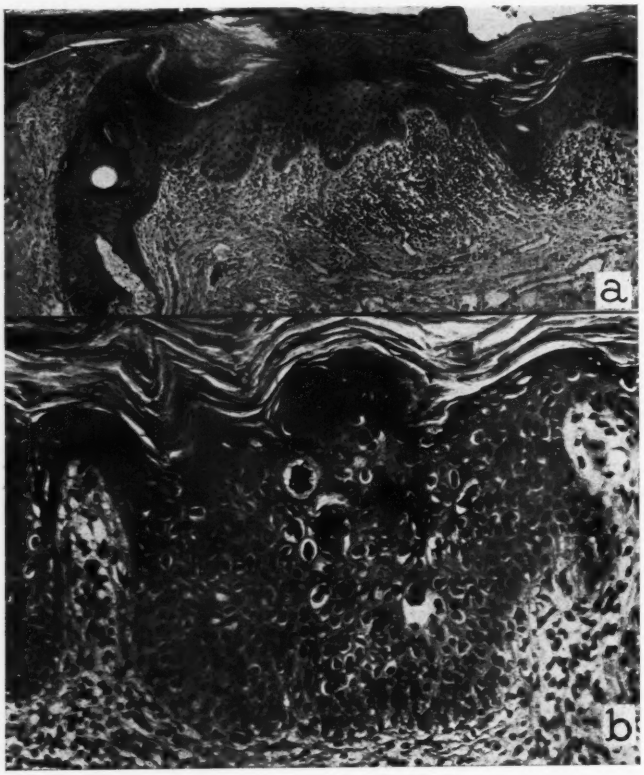

Fig. 7. (*A*) Keratoma senile, back of hand, showing very early squamous-cell epithelioma, Grade 1, *in situ*, with lack of involvement of the sweat duct and hair follicle; (*B*) arsenic epithelioma, back, showing clumping of cells, amitotic cell division, and vacuolization of cells simulating Bowen's disease. Squamous-cell epithelioma, Grade 1, *in situ*.

growth, may simulate imperfectly formed or embryonic hair follicles or sebaceous glands, but without possibility of connecting these growths in serial sections with the mature forms of sebaceous glands and hair follicles to be seen in the same specimen for biopsy. Silver stains, in my opinion, are not of value in distinguishing a basal-cell epithelioma from an epithelioma that originates in a hair matrix, and the presence of melanin does not determine the origin of the basal-celled growth.

Basal-squamous-cell epithelioma represents metamorphosis from basal-cell to squamous-cell epithelioma, and affords further evidence for the origin of basal-cell epithelioma from the basal cells of the epidermis. This denies a fundamental and separate histogenesis of basal-cell and squamous-cell epitheliomas.

The early development of basal-cell epithelioma from multicentric and independent points of origin from the basal cells of the epidermis is best seen and studied in many cases of superficial epitheliomatosis. The presence of mature hair follicles, sweat glands, and sebaceous glands, without evidence of transitional forms, speaks against a hair follicle origin for these tumors.

Basal-cell epitheliomas are seen in 10 per cent or much less of the cases of epithelioma, which are the result of senile keratoses and keratoses from arsenic, tar, and radiotherapy (33), or less than 2 per cent of all the cases of the keratoses from these causes. The greatest majority of these lesions are squamous cell in character.

It is necessary to demonstrate the origin of a given basal-cell epithelioma from the epidermis or dermal appendages by serial section and various reconstruction methods before deciding that it originates from these structures. In regard to arsenic as an etiologic factor, the presence of arsenical keratoses or pigmentation does not confirm that a basal-cell epithelioma is caused by arsenic; in general, one should demonstrate that more arsenic is present in the epithelioma in question than is present in the normal adjacent epidermis.

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CARCINOMA OF THE MOUTH

WITH ESPECIAL REFERENCE TO TREATMENT[1]

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IN frequency, cancer of the mouth ranks second to that of the breast and uterus. It is among the most accessible, yet highly fatal, of cancers, with a mortality rate of from 75 to 90 per cent. The lesions are readily recognizable, yet tend to early disintegration, infection, and regional spread. For example, the frequency of enlarged cervical nodes at the time of admission is reported, for lingual and sublingual cancer, as follows:

	Per Cent	
Iahr	62	
Kuettner	75	
Lenz-Dubois-Roquebert	94	L'Institute du Radium
Menegaux	69.9	103 cases
Quick	50	450 cases of tongue cancer
Roux-Berger and Monod	80	Inoperable or borderline
Sachs	82	

If these figures can be accepted, then, on the average, 73.3 per cent of the patients present themselves with enlarged cervical nodes, whether infectious or carcinomatous no one can reliably predict which.

Mouth tumors are best classified for study according to location, *viz.:*

Cancer labii
Cancer linguæ
Cancer sublinguæ
Cancer gingivæ and mandibulæ
Cancer buccæ
Cancer palati—duri and mollis
Cancer tonsillæ
Rarer types

The lip, tongue, floor of the mouth, and cheek are the sites most frequently involved; the palate and gums are more rarely attacked. By mandibular cancer we understand those cases which, extending from the mucous membrane, gingiva, offer as their chief symptom thickening of the lower jaw bone. They are often diagnosed grossly as sarcoma of the jaw.

Cancer of the maxilla, only as it may arise in the alveolar margin of the upper jaw, is considered. Oehngren's (81) classical review of 187 cases of maxillo-ethmoidal malignancy, the largest series yet reported, clearly demonstrates the effectiveness of radium as an adjunct to surgery, especially electro-surgery of this region.

Treatment of cancer posterior to the faucial pillars, namely, of the nasopharynx and larynx, is indispensably radiologic, with the possible addition of laryngectomy for intrinsic carcinoma of the larynx. Since Coutard (16), in 1921, reported 22 cases, with primary healing in 80 per cent, using heavy doses (5,000–8,000 r) of roentgen radiation through the tissues of the neck, his technic has become more or less standard.

HISTORICAL

Our chief concern is with the rapid changes in therapy since 1900. The Indians, Egyptians, and Persians (1000 B.C.) recognized cancer and attempted to treat it (118). Hippocrates (460 B.C.) knew a great deal about the recognition of cancer, having described many forms, *i.e.*, skin, breast, stomach, cervix, and rectum. He originated the term "carcinoma." His therapy was weak; only caustic pastes and the cautery were recommended.

The first plastic surgery for cancer was done by Celsus (100 A.D.). He removed the breast, and excised cancer of the lip and face.

A century later Galen, the founder of humoral pathology, taught that cancer originated from *atra bilis*, the black bile. He nullified Celsus' approach to the more correct surgical treatment. His bold teachings led away from the scalpel, and limited therapy to the internal and external use of

[1] Undertaken during 1933–1934, Alexander Cochrane Bowen Travelling Scholarship, New York Academy of Medicine.

medicaments, chiefly purgation and bloodletting. For more than a thousand years his teachings were firmly adhered to, *i.e.*, "Nam incurabilia sunt omnia ulcera ex atra bile facta." Corrosive, caustic pastes, and the cautery (ferrum candens) were the sole adjuvants.

Only with the beginning of the nineteenth century were the philosophic systems of the ages and the empirical traditions of the Middle Ages thrown overboard. With the aid of the magnifying lens and the microscope other conceptions of the essence and significance of cancer were reached. By this time the French and German barber surgeons, with knife in hand had long solved the question as to how cancer should best be treated.

Phases in the treatment of cancer of the tongue:

	A.D.	
Paul of Aegina	700	Devised instrument for stilling hemorrhage from the tongue.
Petrus de Marchetti	1664	Extirpation with the hot iron.
Laurentius Heister	1743	First methodical presentation of the medical and operative treatment of tongue cancer.
Inglis	1805	Ligature of the tongue.
C. J. M. Langenbeck	1819	Wedge-shaped excision.
Jaeger	1831	Splitting of cheek.
Mirault	1833	Preventive ligation of arteria lingualis.
Roux	1836	Splitting of mandible.
Regudi	1838	Extirpation from supra-hyoid approach.
Middeldorpf	1854	Galvanocaustic.
Billroth	1862	Osteoplasty—resection of the lower jaw.
Kocher	1880	Extirpation of base of tongue.

In 1829, the Frengh surgeon Recamier first recognized the process of metastasis. He used this term to describe secondary growths in the brain occurring in mammary carcinoma.

William Hunter's discovery, by mercurial injections, in 1746, that the lymphatics were independent of the arteries and veins, led to an intense study of the anatomy of the lymphatics. Injections of wax, lard, oil of turpentine and lavender, gelatin, plaster and alcohol were variously tried. Sappey, a leading French anatomist, in 1874, refined the mercury technic and made anatomic charts of lymphatic areas. At this time the surgeons awakened to the importance of lymphatic drainage for cancer surgery. The earliest radical operations were based on Sappey's charts.

The finest lymphatics were ruptured by the force necessary to inject mercury and wax. In 1896, Gerota (Berlin) obtained clearly the best preparations by injecting a suspension of Prussian Blue in turpentine and ether, using capillary glass pipettes.

In 1898, Kuettner (60), using Gerota's technic on 15 cadavers, filled in the gaps of our knowledge of lymphatics of the tongue, floor of the mouth, and cervical drainage areas. He advised early and wide excavation of the cervical lymphatics in tongue cancer.

In 1900, Dorendorf (29) followed Kuettner's lead by studying in detail the lymphatics of the lip on 20 cadavers, using Gerota's technic.

Crile (26) in 1906, outlined systematically our present "block dissection" technic, which he had performed in 132 cases since 1898. His technic is basically standard today. His operative mortality of 8 per cent in an era of one-stage operations, on debilitated patients, compares favorably with the present rate.

The turn of the century brought the x-ray through Roentgen (1895), and radium through Mme. Curie (1898). Roentgen therapy obtained its first cancer cure when Tor Stenbeck (Stockholm), in 1898, treated a basal-cell carcinoma of the nose that had recurred twice after coagulation with the red-hot iron. Forssell (41) followed that patient until 1920. There was no recurrence.

Soon after the discovery of radium, experiments were made on plants and animals. In 1899, Becquerel carried a tube of radium in his waistcoat pocket for some hours and received a severe radium burn on the underlying skin. This experience led eventually to its use in the diseases of man.

In 1903, S. W. Goldberg (St. Petersburg) applied radium to his own arm. A slowly healing ulcer developed. Suspecting that

radium would have a striking effect on cancerous epithelium, he, together with E. S. London, treated two cases of basal-cell carcinoma of the face, with good cosmetic result. The authors recognized that they had discovered a new and valuable method of treating cancer. The widespread empirical application of radium and x-ray, however, soon burst the bubble of expectancy, and spread a train of failure in its wake. Little success was at first obtained outside the field of skin cancer.

Dominici (28), in 1907, outlined the method of filtration to cut out the softer rays irritant to the tissues. In 1908, he spoke of treating cancer of the tongue with radium, recognizing that the failure of x-rays against tongue cancer was almost complete. In 1910, he announced his method of implanting radium needles in cancer of the tongue. Manifest regression of the tumor, followed by less pain and hemorrhage, resulted.

Further development in France was then held up during the World War. Stevenson (107), in 1914, in collaboration with the Radium Institute of Dublin, first made needles charged with radon emanation. In 1916, he buried fine glass capillary tubes filled with radon, without further filtration, into tumors of the tongue. This method has since been further developed in America, through the work of Failla, Janeway, and Quick at the Memorial Hospital in New York City. According to Quick (87), in 1934, the unfiltered glass seeds used from 1916 to 1925 saved more cases than any other form of radiation, even though at the expense of great suffering because of necrosis. Failla, in 1925, was able to seal emanation in capillary glass tubes with 0.3 mm. gold filter, thus lessening the necrotic action, increasing tissue tolerance to larger intratumoral doses, and thereby overcoming the chief objections to the use of radon seeds. Quick (86), in 1929, reported 450 cases of tongue carcinoma, with 22.4 per cent free from disease from three to ten years, using this method in combination with surgery and cauterization.

However, the use of radon seeds has been little fostered outside of central cancer clinics of America. Regaud, who prefers a constant source of radiation—the element needles—feels that the 0.3 mm. gold filtration is inadequate. To make the filtration 0.5 mm. gold would increase the bulk of the seeds and make their permanent insertion less desirable because of foreign body reaction. Regaud (91), in 1929, reported 344 cases of tongue cancer (from 1920 to 1926), with 23.8 per cent cures for at least three years, using intra-tumoral element needles.

The Radiumhemmet, Stockholm, having large amounts of radium element (10 grams), with comparable results, finds few advantages and little reason for introducing an emanation plant, expensive and complicated to maintain (Ahlbom[2]). Berven (9) reports 278 cases of oral cancer treated, from 1916 to 1926, with 27 per cent five-year cures.

In radiation therapy of intra-oral cancer, since 1910 the pendulum has swung ever more strongly toward the intra-tumoral application of radio-active substances. Since Martin, Quimby, and Pack (69) showed, in 1931, that the minimal lethal dose required for the successful treatment of intra-oral cancer (56 cases) was from 7 to 10 skin erythema doses, if delivered in from 10 to 20 days, the unsatisfactory position of external radiation has been more clearly defined. The intensity of the oral tumor dosage, from an external source, rarely reaches 2 S.E.D., and never exceeds 3 S.E.D. without serious damage to the tissues and often a fatal effect on the patient.

Since 1920, the development of teleradium treatment (mass radiation from a distance, the radium bomb) has been steady. Its wide use in France, England, Sweden especially, and in America has already led to the impression that it is superior to x-ray therapy in the intra-oral field. Its most ardent, reliable proponent, however, the Radiumhemmet, in Stockholm, employs it only in combination with later electrocoagulation, "needling" or surface radium to intra-oral tumors, and as a measure preoperative to dissection of cervical metas-

[2] Personal communication, August, 1934.

tases. Its ultimate usefulness has not yet been ascertained. Its striking effect on carcinoma of the tonsil, in Berven's hands, we shall refer to later.

PATHOLOGIC ANATOMY

Of the malignant tumors of the mouth, epidermoid carcinomas, usually of the adult differentiated type, comprise over 90 per cent. In general, there are two types of cancer of epidermoid origin: the acanthoma, with adult squamous cells, hornification and pearl formation, and basal-cell carcimona, the so-called rodent ulcer. The basal-cell lesion is extremely rare in the mouth. Broders (19), in his wide experience at the Mayo Clinic, has never seen a case. The acanthomas, with varied degrees of hornification, thus dominate the group, plus a few rarer types.

The mouth and urinary tract have a protective covering epithelium, in contrast to the secretory, glandular epitheluim of the gastro-intestinal tract. Hence the buccal epithelium differs from normal epidermis only in its lack of pronounced superficial squamous characters. It has been studied intensively in its relation to carcinoma by Mekie (74) and Fraser (44). Fetal buccal epithelium is composed of a single cuboidal layer. The superimposed prickle cell and keratinized layers in the mature epithelium are regarded as layers of cells in the process of degeneration, without power of multiplication. The cuboidal, basement cell alone has the power of reproduction and of invasion (Ewing, Broders, Mekie). All others are in a stage of degeneration, due to partial starvation and poor oxygen supply. This results from crowding of the intercellular spaces, with diminished play of nourishing intercellular fluids as the cells are forced to the uppermost layers of the epithelium.

Ewing divides epitheliomas of the lip into (1) the papillary, wart-like, slow-growing type, and (2) the ulcerative, infiltrating, more malignant type. The latter lies beneath rather than in the epithelial layer, ulcerates early, with much inflammatory reaction, and may involve the lymph nodes early, which latter, however, seldom become large. The papillary form may eventually infiltrate deeply.

The tongue epithelium is similar to that of the buccal cavity. Fraser (44) could find no structural peculiarity to explain the predominance of cancer in the anterior two-thirds of the tongue. The intra-oral lesion is usually a hard indurated ulcer, sometimes more papillary and nodular. In the tongue the arrangement of blood vessels and lymphatics may somewhat restrict the growth to one lateral half or to the base, but advanced lesions invade both sides, extending from the base in all directions, and from the tip to the floor of the mouth. The tongue edges are the most common locations (Woelfler, 55 per cent; Fraser, 62 per cent), and the dorsum and posterior third are the least.

The majority of lesions of the floor of the mouth are localized around the openings of the salivary ducts, at the side of the junctional epithelium (Fraser). They may show cylindrical cell structure, suggesting salivary gland origin. Tumors arising from the tongue borders and alveolar margin of the jaw are prone to invade the sublingual region. As elsewhere, infection, ulceration, and early progression to the cervical nodes occur. Primary lesions may likewise extend actively to the lip, gums, and tongue as well as to the deeper structures.

Mandibular cancer arises from the gingiva, usually beginning around an infected tooth as a warty ulcer or growth with raised, everted edges. Squamous characters are generally pronounced. It rapidly invades and destroys the jaw, extending to the maxillary antrum if in the upper jaw, or outward to the skin if in the lower jaw. The mandible thickens and is painful, with ulceration usually on its alveolar margin.

The buccal lesion, likewise indurated, is ulcerated and superficial from the first. It extends actively, with much pain and discharge, to invade the loose, thin layer of tissues of the cheek, with fixation of the overlying skin. It arises from fissures, abrasions, and erosions. Lymphocytic infiltration and edema of the submucosa, as

elsewhere, nearly always precede the downgrowth of epithelium.

Malignant tumors of the tonsil, both carcinoma and sarcoma, are more cellular, anaplastic, and rapid-growing as a group. They become infected, ulcerate, and extend widely into neighboring structures without demarcation, and metastasize early. Since 1921, the following classification has been evolved:

Carcinoma
- Squamous-cell epithelioma-adult, resistant, spinal-cell type
- Transitional-cell epithelioma–Lymphoepithelioma } undifferentiated, no keratin or pearls

Sarcoma
- Usually lymphosarcoma.

These will be discussed under the rarer types of tumors.

LYMPHATIC DISTRIBUTION

This determines the chief metastatic paths to the neck. The lymph vessels from the upper lip course right and left to the anterior facial vein, and follow the external maxillary artery through the digastric triangle to the upper deep cervical nodes.

From the lower lip two sets of vessels course to the right and left, without crossing to the opposite side, except in the central lip area. The submucous vessels are the larger, emptying into the numerous small nodes lying close on the submaxillary salivary gland. The smaller subcutaneous vessels empty into the submental nodes. It is important to recognize that the submental, submaxillary, superficial, and upper deep cervical nodes may be involved. Unless the lesion is in the midlip, bilateral or crossed metastases occur but rarely.

So rich are the lymphatic networks of the tongue, floor of the mouth, and neck that metastasis from any mouth tumor may deposit in any node of the neck. The lymphatics of the anterior half of the tongue have separate origin from those of the base, yet all paths lead to the cervical groups. Cancer of the tongue seems to involve the upper deep cervical group primarily, whereas cancer of the floor of the mouth first attacks the submaxillary group (Woelfler). Cancer at the tip of the tongue or sublingually near the frenum passes first to the submental and sublingual groups, and may involve the deep cervical nodes bilaterally.

There are four cervical lymphatic groups of special interest. The lingual and submental nodes lie on the mylohyoid muscle and between the genio-hyo-glossal muscles. They are part of the system that drains the lip, anterior tongue, and buccal floor.

The submaxillary group lie principally in the digastric triangle, are adherent to the capsule of the submaxillary salivary gland, and are continuous with other nodes that extend as far back as the parotid gland. This group drain the border of the tongue as far back as the fauces, the central part of the anterior half of the tongue, and the under surface of the tip and floor of the mouth.

The superior deep cervical group lie on the sheath of the internal jugular vein and on the carotid artery, extending upward as far as the base of the skull, and draining all parts of the mouth, tongue, fauces, and upper pharynx. The largest and most important node lies at the bifurcation of the common carotid or slightly higher. Anastomosing with this group is a small cluster of nodes at the lower pole of the parotid, which drain the anterior surface of the palate.

The inferior deep cervical nodes lie on the jugular vein at the crossing of the omohyoid muscle and extend down behind the clavicle. They receive branches directly from the apex and base of the tongue. The terminal branches empty directly into the jugular and subclavian veins, independent of the thoracic duct, on the left side. Both the deep groups are more or less covered by the sternomastoid muscle and are adherent to the deep layers of its sheath.

RARER TYPES

The majority of intra-oral malignancies arise from the buccal pavement epithelium. The rare exceptions are:

Sarcoma.—Soft-part sarcomas of the mouth, if giant-cell epulis is excluded, are very rare. They are mainly the round-cell type. The newgrowths arising from bone, *i.e.*, medullary or periosteal sarcoma, or tumor-like osteitis fibrosa are much more frequent. The latter occur in younger age groups, and equally in both sexes, as opposed to carcinoma.

Lymphosarcoma.—This type occurs more frequently in the nasopharynx.

Nerve Cell Tumors.—These are neurofibroma, neurinoma, and glioma—even rarer.

Transitional-cell Epithelioma.—In 1927, Quick and Cutler (85), from a large series of cases of intra-oral cancer, selected 20 cases which had shown striking regression of the tumor after small doses of external radiation. They found that these tumors had a peculiar histologic structure. The cells resembled transitional epithelium; they lacked the flat pavement characters, spines, hornification, and pearls of the usual squamous growths. The tumors were most common in the base of the tongue, tonsil, and pharynx, where transitional epithelium has been found.

The diagnosis is difficult. They are confused with branchiogenetic carcinoma, endothelioma, lymphosarcoma, and reticulum-cell sarcoma. Ewing (37), studying 300 intra-oral tumors, stated (1929) that "the more rapidly growing forms I find difficult and almost impossible to differentiate from other forms of carcinoma." Berven[3] believes these tumors to be indistinguishable both clinically and pathologically from sarcoma. Of Quick's and Cutler's original 20 cases, 13 died within 18 months. The remaining seven had not yet reached that limit.

Lympho-epithelioma.—In 1921, Schmincke (99), of Munich, and Regaud, of Paris, independently called attention to certain oro-pharyngeal tumors, usually diagnosed as sarcoma, whose histologic characteristics consisted of embryonal epithelium growing in intimate association with lymphocytes. They believed that the epithelium covering the lymphoid deposits of the nasopharynx, especially of the tonsil and base of the tongue, was fundamentally modified by a symbiosis with the lymphocytes; also, that this tissue should be regarded as a specific organ, called lympho-epithelium (Jolly), giving rise to a specific group of tumors.

Schmincke reported 10 cases, describing five convincingly from the histologic and embryologic standpoint. He holds that the lympho-epithelium and its tumors arise from the entodermal epithelium of the pharyngeal pouches as do the tonsils and thymus gland, all three having reticulo-syncytial-epithelial structure intimately penetrated with lymphocytes.

The lympho-epitheliomas are all embryonal, hence their extreme radiosensitivity. Ewing regards the lympho-epithelium as definite, "but more work must be done to define the tumor group."

Carcinoma of Cylindrical-cell Origin.—This type usually occurs in the floor of the mouth. It arises probably from salivary gland tissue.

Mixed Tumors.—These are most common in the soft palate.

Epulis.—Is this a tumor? Kaiserling (52) regards epulis as a granuloma, a productive inflammation characterized by giant cells, usually cell-poor, though it may be so cellular as to be confused with sarcoma. He suggests removing it from the true tumor group.

It is recognized clinically, however, as "semi-malignant." It tends to recur locally and to metastasize; it may be histologically benign and clinically malignant; its structure varies between a firm fibroma and a sarcoma, both of the giant-cell type.

Grossly, it appears as a pedunculated growth with narrow pedicle—projects between the teeth—arising from the periosteum of the alveolar margin or from the peridontium. It is dark bluish-red, covered with mucous membrane. It may perforate and bleed easily. The etiology is unknown. The lesion is common between the ages of 20 and 40 years.

The fibrous type responds poorly to

[3] Personal communication, September, 1934.

radiation and, hence, should be generously excised. Though the cellular type may respond well, the painful, slow-healing radio-osteitis that may easily occur restricts the use of radium (1–2 needles) to be followed by excision. The frequency of recurrence after excision must be kept in mind. With the bone drill and Gigli saw a partial segment of the regional mandible may be removed. Berven,[4] using surface radium, failed to obtain primary healing in 30 per cent of his cases. These went on to malignancy, developing neck metastases. Because of the difficulties of proper surface application he now implants needles.

Johnson (57) states that the treatment is emphatically not by irradiation alone but by cautery removal and irradiation of the base of the wound.

Adamantinoma.—The so-called epithelial (rather than cystic) odontoma is composed of masses and anastomosing strands of epithelial cells which are believed to originate from an enamel organ or from islands of epithelium, the paradental remains.

The cystic types are often benign, while the solid are destructive and invasive.

ETIOLOGY

The direct cause, as for cancer elsewhere, is not known. A confusing mass of information has been gathered about associated conditions which seem to influence the appearance and course of the disease. Syphilis, the use of tobacco, leukoplakia, and defects of the teeth play the important part. In many cases, all of these may be present.

Syphilis.—While this has been exaggerated as an etiologic factor (Bloodgood, 13), it is important for the following reasons:

(1) Because of its high incidence in mouth cancer (Simmons, 16 per cent, Fraser, 14 per cent, and especially in cancer of the tongue, Ehrlich, 30 per cent, Berven, 30–35 per cent, Quick, 35.1 per cent, and Judd and New (27) believe it to be even higher).

(2) Because of the changes it causes in the tumor bed, rendering the tumor markedly resistant to all forms of radiation and to surgical healing.

(3) A positive Wassermann may mask the diagnosis of cancer coincident in the same lesion, with loss of valuable time.

If present, syphilis almost always exists in the same ulcer as the cancer of the tongue (Judd and New). In every mouth ulcer, regardless of the Wassermann reaction, cancer can be excluded only by biopsy. Specific treatment should be begun at once.

Tobacco.—This is a local or general irritant rather than the drug producing the disease. Mouth cancer preponderates in males to the proportion of eight to one, most of them being strong smokers. In Broders (18) 537 cases of lip cancer, 78.5 per cent were *pipe* smokers. Ludwig found that the same dry products of combustion occur in tobacco smoke as in soot, tar, and paraffin.

Leukoplakia.—Without question this, especially the warty type, is a pre-cancerous condition. It is an inflammatory lesion, seen particularly in smokers and drinkers, with syphilis present in from 45 to 90 per cent of cases (Kaiserling, 52). It is present in four or five of every 100 men under 40 years of age (Ducuing, 29-*a*), and is ten times less common in women.

These "smokers' patches" occur preferably on the anterior dorsum and edges of the tongue, also on the lip and buccal mucosa, near the angle of the mouth. Fissures may occur. The lesion develops slowly as a spotty thickening of the buccal epithelium, with marked keratohyalinization. The underlying submucosa in the early stage shows chronic inflammation, edema, with distended venules, loose fibrous tissue, and lymphocytosis. The papillæ are increased and elongated. In pure old cases the inflammatory changes are scarcely demonstrable. According to their age, the plaques are cloudy gray or shiny mother-of-pearl, mostly sharply bounded, with a narrow red border. There is often great difficulty in differentiating the lesion from beginning cancer. Often the basal-cell layer is no longer sharply outlined. Atypical downgrowths of epithelium may occur.

[4] Personal communication, September, 1934.

Clinically, there is at first slight burning, with superficial white spots. The tongue may become stiff. Swallowing and speech may be difficult. Elevation and cornification of the lesion ensue, followed by fissures, bleeding, a typical downgrowth of epithelium, carcinoma.

Fournier (43), in 1900, in studying 324 cases of leukoplakia buccalis found that in 30 per cent of the cases leukoplakia went over to cancer. Of 95 tongue cancers, 65 had both leukoplakia and cancer; 259 cases had syphilis.

Leukoplakia leads all other pre-cancerous lesions in importance. Every case is curable. It should be treated without delay, at first conservatively, *i.e.*, clearing up of mouth and gastro-intestinal disorders. When the lesions are early and not extensive, magnesium sulphate one gm. in one liter of water, taken in amounts of one glass three times daily, should show improvement in three weeks. The older lesions should be removed with the electrothermic loop to a depth of a few millimeters, under local anesthesia, in the clinic or office.

Defects of the Teeth.—It is common knowledge that cancer has frequently developed at the site of long-standing direct irritation from a broken, sharp-edged tooth or from an ill-fitting denture.

Mouth Infection.—This is the most constant finding, occurring in 50 per cent of the cases. Papillomas, fissures, chronic glossitis with hypertrophy and thickening, ulcers of any type should be recognized as precancerous states. Judd and New have reported five cases with pre-existing actinomycosis.

Heredity.—This plays no important part. The sporadic cases reported seldom exceed 2 per cent.

Alcohol.—This may play its part as an irritant. The incidence of mouth cancer is higher in countries where the drinking of raw spirits is prevalent (Fraser, 44).

DIAGNOSIS

The lesion is usually a hard indurated ulcer, sometimes more papillary and nodular. Except for lesions of the posterior tongue, the diagnosis of cancer on the foundation of biopsy should be readily made. Tongue cancer posterior to the circumvallate papillæ is difficult both for the patient and the physician to recognize. Any ulceration of the mouth of more than two weeks' duration should be investigated from the cancer standpoint.

The first symptom may be enlarged cervical nodes. While these may be inflammatory, they should be regarded as cancerous in the treatment of the patient. Once cancer invades the cervical nodes the chance for cure is practically lost. Mekie (74) found, in 268 collected cases of mouth cancer with cancerous neck nodes (cases of Forssell, Quick, and his own—1932), only 8 (or 2.79 per cent) cured. Simmons (103), in 376 cases of mouth cancer, reported 5 per cent surgical cures in patients with clinical metastases and none by radiation (which was admittedly inadequate in dosage). Further, he states that even in early cases no reliance can be placed on the presence or absence of cervical nodes as an index of metastasis.

This meager chance of cure, once the neck nodes are invaded, should be meditated seriously by those who would temporize or moderate the treatment of the cervical lymphatic areas in primary cancer of the mouth. Bloodgood (13) sounded the important note in 1921, stressing propaganda for earlier diagnosis by education of the public, the medical and dental professions, stating that this can save more lives than any improvement in surgical technic, x-ray, radium, or cautery.

The differential diagnosis is generally well controlled by the free use of biopsy, followed by treatment without intervening delay.

Simple ulcers from pressure of teeth or plates may be found.

Leucemia.—This may cause gangrenous ulcers of the mucous membrane (ulcerative stomatitis), swelling of the lymph nodes at the base of the tongue, plus bleeding gums.

Agranulocytosis.—This, with mouth ulcerations, may be differentiated by the more acute systemic prostration plus leukocytopenia.

Tuberculosis.—This as a mouth disease is much rarer than syphilis, in spite of the fact that the possibility and frequency of mouth infection with tubercle bacilli is greater than with spirochetes. However, tuberculosis is fairly common in the tonsil (Burnam).

Actinomycosis.—This arises usually by injury to the soft parts by hard grains, and may form a small tumor mass, usually at the tip or edge of the tongue or floor of the mouth. It can awaken the suspicion of cancer; it is also confused with gumma and tuberculosis. The diagnosis is made by the yellow transillumination, the superficial site in the mucous membrane, the pea size, and the granules of yellow *Actinomyces.*

Diagnosis from the pathologic picture alone has its limitations. At times, even the most practised histologist cannot decide between chronic ulcer, syphilis, tuberculosis, and cancer, when there is a typical downgrowth of epithelium. Borst and Kaiserling (52) are astounded at the ease with which atypical epithelial growth, leukoplakic hyperplasia, and cancer are differentiated. They are likewise astonished at the scanty histologic evidence, believing that this may be a factor in the more favorable results reported.

PATHOGENESIS

Generally the degree of malignancy increases as one passes from lip to pharynx. Tumors of the mouth are chiefly of the adult, differentiated type. The added factors of decreasing accessibility to treatment, increasing vascularity of the tumor bed, association with vital structures, and the activity of the muscles of the tongue and floor of the mouth favor spread of the disease. Thus malignancy is seen to be lowest in lesions of the lip and cheek, and progressively higher in those of the tongue, floor of the mouth, and tonsil.

Spread of the disease occurs by direct extension and chiefly by metastasis. It is generally accepted that the latter occurs by embolic dissemination of the tumor cells, usually through the lymph channels. Evidence of spread *via* the hematogenous routes is scanty. Single cases of implantation metastasis in the esophageal, gastric, and duodenal mucosæ after cancer of the tongue (Von Bergmann, 112, 1881) and in the bronchial nodes by aspiration (Lenz and Sproul, 65, 1934) have been reported. Secondary transplant by contact, *i.e.*, cancer of first the lower, then, five weeks later, of the upper lip at the point of contact (Von Bergmann), and of the cheek in contact with tongue cancer, have been sporadically reported.

Metastases from oral cancer are regional rather than remote. They are most always confined to the barrier of the cervical lymphatic groups. Remote metastases are very rare. Crile (26), in 1906, found less than 1 per cent in 4,500 statistical cases.

The clinical course is usually progressive, to become fatal in the average of two years—somewhat longer for cancer of the lip. The course is more rapid in the lingual cases, commonly from 6 to 12 months, and in pharyngeal tumors, from 4 to 10 months. Most metastases seem to have arisen from 5 to 6 months after the perceived onset of cancer of the tongue (Berven and Simmons). The local and regional growths become secondarily infected, usually streptococcic, with necrosis and suppuration, toxic systemic effects, and emaciation. The chief causes of death are pneumonia, septicemia, edema of the glottis, and hemorrhage. Ewing (35) stresses the frequency with which secondary infection with the streptococcus complicates or dominates the later stages.

ESSENTIAL PRINCIPLES OF RADIOTHERAPY TO PRECEDE SURGERY

Treatment resolves itself into the use of surgery (electro-surgery) or radiation, or both. The problem so difficult to-day is to see in its proper light the value of the innumerable combinations of radiotherapeutic measures proposed. The results of presumably good radical surgery (Kuettner, Crile, Bastianelli, Zweifel-Payr), carried out during the preceding thirty-five years (1898) seem fairly well standardized in yielding the absolute rates of between 10

and 20 per cent, averaging 15 per cent of five-year cures.

We have seen that since 1910, roentgen and radium therapists have increasingly taken over the radiation of intra-oral cancer. We hear repeatedly that there can be no standard uniform dosage against carcinoma or sarcoma because of their great variations, and because of the varied reaction of the tumor bed. However, it is felt here that the *rationale* of effective radiation therapy of intra-oral tumors can be placed within definable, workably uniform limits.

First of all, the selective action of the roentgen and radium rays has been given thorough trial in the intra-oral group. By selective action is meant the administration of dosages sublethal to the adjacent normal tissues, yet causing disappearance of the tumor. This selective action shows its effect best on the undifferentiated embryonal tumor types, which, except in the tonsil, are rare in the mouth. We have seen that the usual adult epidermoid carcinoma requires for its destruction at least from 7 to 10 S.E.D. to all parts of the growth, whether x-ray or radium be employed. This dose is definitely lethal to normal epithelium and connective tissue. Thus for the reliable destruction of intra-oral tumors, the caustic rather than selective action of radium is largely called upon.

Secondly, external radiation, limited by the maximum tissue tolerance of 2.5 S.E.D., *per se*, cannot approximate the intensity dosage required for effective treatment of either the primary or metastatic lesions of the intra-oral group. As a preliminary, adjuvant measure it has a place, not to be over-evaluated.

Roentgen and radium rays belong in the series of electro-magnetic ether waves. On living tissues both act not as heat, producing inflammation and necrosis, but they injure the vitality of the cell, causing slow death. The younger the cell, the more intense the effect. Theoretically the correct dose injures only the tumor cells. In other respects roentgen and radium rays are quite different. Roentgen rays are produced by electric current in a vacuum tube; radium rays arise from destruction of the radium atom, yielding emanation. The end-product of radium destruction is non-radiant lead.

Radium and its salts give off three kinds of rays—alpha, beta, and gamma. Alpha rays, composed of atoms of helium, are cast off the radium molecule. They have feeble activity and are all arrested by the container of the radio-active substance. Beta rays are composed of electrons and are of considerable vitality. They are comparable to cathode rays and are arrested by a thickness of 0.1 mm. of gold or platinum. The alpha and beta rays are important therapeutically only in their injurious effect upon tissue, causing necrosis; hence they should be excluded as much as possible.

The gamma ray is very different. It is a vibratory type, has the same quality as the x-ray, and has essentially the vitality of light. But the wave length is infinitely shorter than that of the x-ray (0.017 Ångstrom unit), and these rays are much more penetrating. Just as for x-ray, there are in the gamma radiation an infinity of rays of different wave lengths of unequal penetration. These softer rays are cut out by increasing the thickness of the filter to 1 mm. of platinum.

When a gamma ray falls on an object this emits a new radiation, *i.e.*, a secondary radiation of softer rays having injurious, necrotic action. The hardness of these secondary rays rises with the atomic weight of the secondary radiator, *i.e.*, slight from loose connective tissue, hard from bone. To diminish secondary radiation of the tissues, the radium tubes should be placed as far as possible from substances with high atomic weight, namely, bone, to avoid necrosis.

The first experimenters used the necrotic action of beta and soft gamma rays in tumoral therapy. This is to be avoided for necrosis favors infection, the danger of hemorrhage is increased, and the tumor is replaced by an ulceration of radionecrosis, with little tendency to cicatrization.

Most therapists to-day use only the hard gamma rays. Some filter with more, others

with less, but all, except those using radon seeds, use at least 0.5 mm. of platinum, which stops all the beta and part of the gamma rays.

The emanation, radon, namely, the first degeneration product of radium, may be collected and used in containers. It gives off the same quality of radiation but for a short time only, losing 50 per cent of its intensity in four days. The use of the element is more widespread and preferred because of its constant source of radiation. Failla's ingenious apparatus for collecting and sealing the emanation in gold filtered glass tubes has made the use of radon practicable in larger cancer clinics.

RADIATION REACTION

Following the application of radium, Ewing (34) describes the following more or less specific sequence of events: *From three to five days later*, hyperemia, lymphocytosis and polymorphonuclear leukocytosis, and swelling of all the cells; *second week*, the tumor cells are characteristic, with enlarged cell bodies, swollen, homogeneous, hyperchromatic nuclei; hydropic vacuoles in the cytoplasm and fusion of the giant cells; *third week*, the number of cells is reduced; liquefaction necrosis, invasion and compression by lymphocytes, and a proliferating stroma are seen; *fourth and fifth* weeks, only pyknotic nuclei and an occasional giant cell are seen; the stroma is active, and is impregnated with capillaries, leukocytes, plasma cells, and polyblasts. Eventually all becomes granulation tissue, followed by re-epithelialization. All variations of the above may occur.

The reaction of normal tissue, of the tumor bed, together with the direct action upon the tumor cells, determines largely the response of the tumor to radiation. Arteriosclerosis and syphilitic changes of endarteritis and fibrosis in the tumor bed diminish radiosensitivity and retard afterhealing. Infected and necrotic tumors react less favorably. In fibrous and nonvascular areas the defense reaction is poor. Re-activated tumors, previously treated with inadequate amounts of radiation, show increased resistance to further radiation. Repeated doses cause cicatrization, ulceration, immobility, constriction of vessels, nerves and hollow organs, pain and distress (Ewing). For these reasons adequate radiation should be given at one sitting or within one short period.

TREATMENT

It is imperative that treatment of the primary lesion and treatment of the regional cervical lymphatic areas be carried out without delay. It is quite generally agreed that small, early, easily removable lesions of the lip and mouth may best be excised. Advanced, inoperable lesions without question should be radiated. It is with the large intermediate group of operable and borderline cases that great confusion exists as to management.

Oral hygiene under supervision is important. This may be done during the period of preliminary external radiation. All areas of infection in the mouth should be corrected. Removal of septic teeth and painting of the gums night and morning with equal parts of tincture of iodine and tincture of aconite, plus frequent mouth washes, are recommended. Tobacco and alcohol should be reduced to a minimum. Anti-syphilitic therapy may be begun at once.

CANCER LABII

There exists no doubt to-day that the primary lesion can be effectively destroyed as well by varied forms of adequate radiation as by surgery. Radiation is preferred by many because of greater conservation of surrounding normal tissue, and, with re-epithelialization, less deformity and a better cosmetic result. This we believe to be true, judging from the controlled experience of the Radiumhemmet, in Stockholm, where the interstitial method has been routinely employed in cancer of the lip for eight years (since 1926).

Lesions of the lip under 1 cm. in size may be excised without marked deformity. For lesions over 1 cm., wide excision may be done, with plastic repair in cases in which

it is necessary, or the proved methods of radiation, as carried out by the larger, controlled clinics, may be employed.

The following methods of radiation may be employed: the minimum lethal dose of from 7 to 10 S.E.D. may be administered by x-ray, with light filtration (1 to 2 mm. Al) and careful screening of the surrounding tissues; surface radium *via* molds to all three accessible surfaces of the lip, or the implantation of radium needles. The latter method is recommended here, based on the experience of the Radiumhemmet, in Stockholm. A standard technic has been evolved which is easy of application, has a comparably low percentage of recurrence, and is relatively free from technical difficulties. Forssell (40) reported 68 per cent absolute cures in 66 cases, which compares with the 60 to 70 per cent generally reported [Arzt and Fuhs (1), Broders (18), Collins (25), Kennedy (58), Pfahler and Vastine (82), Quick (86), Regaud (90), Steiner (35), Widmann (117)].

TECHNIC

For lesions of the lip (and skin) up to 3 cm. in diameter, one treatment should consist of the following: (1) local anesthesia, biopsy; (2) insertion of usually six needles with thread attached (each containing 10 mgm. of radium element, filter equivalent to 1 mm. Pb, length 2 cm., thickness 0.25 cm.), placed 0.75 cm. apart, for four hours); total dosage would amount to 6 needles $\times$ 10 mgm. $\times$ 4 hr. = 240 mgm.-hr.; (3) the needling is facilitated by first inserting a thin, double-edged blade to prepare the bed for the needle.

Usually no further treatment to the primary lesion is required. This is followed in a few days by progressive inflammation, leading to ulceration at ten days, with reepthelialization well marked at three weeks after treatment. The end-result should be a soft, non-pigmented, smooth scar. Any induration raises the suspicion of persistence of the disease, demanding additional—though less intensive—treatment.

Variations of the above technic, of course, occur, depending on the size and thickness of the lesion. A second set of weaker needles (3 mgm. each) is also used, eight being inserted as a rule. On one occasion, the infiltrating lesion being 2 cm. in width and depth, the maximum number of 15 needles, each of 10 mgm. element, were inserted in two layers, for four hours, giving a total dosage of 15 $\times$ 10 mgm. $\times$ 4 hr. = 600 mgm.-hr. The end-result was not seen.

For lip lesions larger than 3 cm., distant radiation by x-ray or teleradium (the five-gram bomb at 3 cm., giving depth dosage of 2 cm.) is preferred. Needling of such large lesions involving the entire lower lip gives too great an area of necrosis and ulceration, which may be aggravated by secondary infection, and usually leads to a poorer end-result. Massive resection, with plastic repair, has proved effective with such lesions.

Lesions of the upper lip, occurring so rarely as to lead some to believe that an immunity of the area exists, may be treated as above. Primary healing will result in over 90 per cent of the cases under skilled x-ray, surface or interstitial radium, electrocoagulation or surgical treatment, or any planned combination of these.

CANCER LINGUÆ

Here we are dealing with the most common and one of the most malignant tumors of the mouth. A frontal plane through the circumvallate papillæ and the seventh tooth of the lower jaw divides the anterior half from the base of the tongue. Lesions of the anterior half may be treated by excision, electrocoagulation, radiation, or by a combination of these. With excision, less than hemiglossectomy is usually considered unsafe.

Radiation here signifies emphatically intratumoral radium. Surface radium has no place in the treatment of intra-oral cancer, no matter how heavily filtered (Quick, 87). To give the desired lethal depth dose may result in gross permanent damage on the surface, with painful, unstable radium burn scars. External radiation by roentgen rays or teleradium may be used as pre- or post-auxiliary measures, but should not be relied

upon to accomplish more than partial regression of the lingual tumor, regardless of the extent of cross-firing. Intratumoral radium, whether the element or emanation, has found the widest acceptance as the most reliable method of delivering the required epidermicidal dose to all parts of the lingual cancer. Tables have been formulated according to which, by measuring the diameter of the tumor, the amount of radon (in seeds) required to give the desired dose may be ascertained, expressed in erythemas (Martin, Quimby, Pack, 69).

In 1923, Regaud (89), in Strasbourg, presented startling results, namely, 24 cures of at least two years' duration by radium puncture of cancer of the tongue. In his London report, in 1925, 20 of these patients were still alive and free from disease. These results were acclaimed as the best ever reported (Muir, 78). Only one patient had died of recurrence. Subsequent developments of Regaud's technic have led to its present-day wide adoption. He has called attention to the instability and increased radiosensitivity of the cancer cell during mitosis. On the basis of this conviction he has formulated the principle of using small doses (weak needles) of gamma rays only, delivering the epidermicidal dose over a long period of time so as to radiate all the tumor cells in their mitotic phases. His technic, described by Lenz (64) and Muir (78), has varied recently only in the increased emphasis on teleradium as a pre- and post-supplement to the implantation of needles, and as a method of treating neck nodes prophylactically (see Treatment of Cervical Nodes, p. 40).

TECHNIC

(1) A single treatment is given which is usually preceded and followed by external radiation (teleradium). The needles used should be 2.7 and 3.5 cm. long; 1.5 mm. thick; filtered with 0.5 mm. platinum; contain 0.6 to 1.0 mgm. element; 1 needle per c.c. tumor tissue; for from six to eight days, usually eight. Total dosage, 1,500–3,500 mgm. hr., according to size of lesion. Each needle has a double eye, so that it may be fixed in the tissue by suture; the other thread is strapped by adhesive tape to the cheek. There should be daily mouth irrigations. A fluid diet must be followed.

This prolonged single treatment must not exceed a certain limit of time, for the growth may become resistant, *i.e.*, retrograde changes in the tissue, obliterative endarteritis, making the tissues susceptible to infection and radionecrosis.

The above method has been adopted with approval by Handley (49), Cade and Evans (33), Harmer and Russell (50 and 51), Lenz and Muir, among others. If the growth has not disappeared in six weeks, Harmer excises the regressive lesion with endothermy.

Berven[5] and Quick (87) see no special advantage of weak radiation over long periods. Since 1922, at the Radiumhemmet, Berven has given: (1) External radiation by teleradium, using the 5 gm. bomb at 6 cm., through four circular portals, by cross-firing above and below the mandible, giving from 50 to 100 gram-hours total dosage. After from three to six weeks the reaction has largely subsided. Partial regression of the tumor occurs in 75 per cent and total disappearance in approximately 25 per cent of the cases. (2) The tumor remnant is either destroyed generously by bipolar electrocoagulation, followed by implantation of needles into the tumor base, or the remnant is needled with 10 mgm. needles for four hours, as outlined for lip cancer.

Quick (84 and 87) prefers the use of 0.3 mm. gold tubes of emanation, preceded by "thorough" external radiation. This cuts down the intensity of the interstitial dosage required. He feels that tubes of less than 1 mc. radon do not provide enough gamma radiation per unit. The principle of 1 mc. seed per c.c. of tumor tissue is generally followed.

During each intra-oral treatment with radium a suitable shield of lead covered with dental compound should be molded, thereby protecting other parts of the mouth.

It must be remembered that implanta-

[5] Personal communication.

tion of the tumor bed after excision with the knife or cautery delays healing, often from two to three months.

For cancer of the tongue arising on leukoplakia, the best treatment is excision (Lenz, 64). In general, leukoplakia persists at the site of an epithelioma that has been cured by radium, unless radionecrosis destroys this site. Saracin (98-*b*) found leukoplakia present in 20 of 30 cases of consecutive (multiple) cancer of the buccal cavity. Further, tongue cancer superimposed on a syphilitic tumor bed responds badly to radiation and the prognosis is usually worse (Berven).

Treatment of tumors of the base of the tongue is difficult with all methods. The region is inaccessible to effective surgery. The nine patients cured for four years in Rieder's (93) series of 82 tongue cases treated surgically, all had lesions of the anterior third of the tongue. The remaining 73 cases died within the four-year period.

The difficulties of implanting radium needles are also considerable. This has led to suggestions of inserting weaker radon seeds—0.5 to 1.0 mgm., with 0.3 mm. gold filtration, totaling not more than 10 mgm. (Souttar, 106)—through the neck, beneath the ramus and behind the angle of the mandible, with care not to penetrate into the oral cavity because of the danger of rapid spread of infection. Cade (33) advises resection of the angle and ascending ramus of the mandible for exposure to insert needles in the base of the tongue and posterior mouth. He states that the after-function is good.

Láng (63), of Budapest, recommends inserting needles through the neck, above the hyoid bone, into the base of the tongue. He first cocainizes the pharynx and controls the insertion by placing a finger in the pharynx. The needles (strength not stated) are left from five to six days. If the tumor is extensive, a suprahyoid linear incision is made and the entire extent of the growth is needled. By this method he obtained primary healing in five of eight cases of cancer of the base of the tongue. Lasting results are not mentioned. Needles inserted into the tongue through the mouth should, of course, be fixed by suture so as to prevent loosening or swallowing of the needle.

Regaud, Berven, and Quick stress the importance of thorough external radiation as a preliminary measure. The task of preoperative radiation, as described by Forssell (40), is, besides its direct effect on the tumor tissue, to diminish peri-tumoral infiltration by calling forth a resorption process, and to facilitate radical operation, occasionally changing an inoperable to an operable tumor. In addition, it may weaken the virulence of the tumor and thereby lessen the danger of dissemination by surgery.

CANCER SUBLINGUÆ

Cancer of the tongue, floor of the mouth, and of the lower jaw often merge into one another by extension. The consensus as to treatment of sublingual cancer heavily favors radiation. Radical extirpation is difficult. Judd and New (27) employed the Kocher operation, *i.e.*, splitting of the mandible close to the midline and radically dissecting the floor of the mouth and the cervical lymphatics, in six advanced cases, all of which died of recurrence. Kuettner obtained 11 per cent cures of sublingual cancer in his series of 266 cases of mouth cancer (Hahn, 47). Eggers (31) removes the primary with the electrocautery, after first ligating the lingual or external carotid artery.

Regaud and Berven employ the same technic as separately described for cancer of the tongue. Intratumoral radium, heavily filtered, with sub-lethal amounts in the region of the mandible, is advised. Danger of bone necorsis is great from the dose necessary. Regaud (91) reports 22 per cent cures in 77 cases. Berven (5) reports 26 cases, from 1913 to 1925, of which seven were cured and 19 were dead. His 11-year report, from 1916 to 1926, showed:

FIVE-YEAR CURES

Lingual cancer	32%	278 tumors of the mouth with 76 (or 27 per cent) five-year cures.
Sublingual	34%	
Mandibular	18%	
Buccal	26%	

Láng reported primary healing in seven of ten cases, by needling both through the oral and submental routes, without mention of end-results.

CANCER GINGIVÆ AND MANDIBULÆ

Radiation here offers little. While a few authors advise preliminary application of local surface or interstitial radium (Rose and Phillips, 95), Berven, 5 and 8), these and others favor ultimate resection of the mandible, especially when the bone has been destroyed by irradiation, as is frequently the case (Blair, 11, Quick, 87, Forssell, 41, Regaud, 64, and Simmons, 4). The difficulties of radiologic treatment are great. The periosteum is exceedingly sensitive to radium. The ordinary dose causes necrosis in which cancer may grow rapidly (Berven, 5). Radiated bone becomes osteomyelitic. The sequestration is so slow and painful that early resection of the involved bone is indicated. Berven first applies teleradium pre-operatively, then coagulates the lesion with endothermy, with later resection, as necessary.

When the alveolus is invaded, Rose and Phillips (95) first insert small element needles of from 1 to 2 mgm. strength for from seven to ten days, until the "optimum reaction" occurs, *i.e.*, hyperemia, softness, and white plaques of lymph on the surface. Then the involved section of bone is removed with the drill and Gigli saw so as to leave a bridge of continuity of the mandible.

Cancer arising in the gingiva or alveolar margin of the upper jaw may extend to involve the maxillary antrum. Destruction by electrocoagulation is recommended, followed by packing radium into the wound, if it is extensive. Oehngren (81) employs four tubes, each of 25 mgm., with the heavy filtration equivalent of 3 mm. Pb, laid in the wound for from 15 to 20 hours, giving a total dosage of from 1,500 to 2,000 mgm.-hr. Oehngren's work is stressed as authoritative in the treatment of maxillo-ethmoidal cancer.

CANCER BUCCÆ

The best results are obtained with lesions of the lip and the cheek. Destruction by the knife, electrocoagulation, or interstitial radium may be employed, preferably either of the latter two. Pólya (83), with wide experience in plastic surgery of this region, warns that extensive removal of the buccal mucous membrane leads to scar formation, contraction, and inability to open the mouth.

If the lesion is to be radiated, certain points must be kept in mind. The bucca is thin and has poor resorptive powers. It is technically difficult to protect the gums and alveolar process. The danger of overdosage and necrosis is great. It is important to ascertain whether or not the skin over the cheek is fixed. Láng could not cure any of these with interstitial radium. Surface applicators should not be used, for they are difficult to apply and hence are dangerous (Berven, 4). The buccal mucous membrane is very sensitive as compared with the resistant buccal cancer. Perforation of the cheek, with persistent salivary fistula, is a dire complication. Superimposing even the slightest procedure on heavily radiated tissue, especially in this region, may lead to perforation.

As least dangerous, Berven recommends external radiation (teleradium) followed by either electrocoagulation or insertion of radium needles, 1 mgm. for each 0.25 c.c. of tumor tissue. If the pterygoid muscles are invaded, with partial fixation of the jaw, Láng inserts needles first into the anterior part of the tumor, and later completes the implantation when partial regression has occurred, affording better exposure.

CANCER PALATI

Cancer of either the hard or soft palate occurs but rarely. The hard palate may be invaded by tonsillar tumors. Destruction by electrocoagulation, followed by radium laid in the wound packed with gauze, would seem the rational approach. Palatal defects may later be compensated by the wearing of a suitable artificial plate.

With cancer of the soft palate, Láng obtained primary healing in three of five cases by using 1 or 2 mgm. gold filtered element needles interstitially. Souttar (106), rec-

ognizing the inconvenient access to the palate, feels that it can best be approached from behind the angle of the jaw. This area lies in the plane of the soft palate; hence, the needle can enter any point of the soft palate on the same side without entering the mouth. He advises the use of weak radon seeds, totaling not more than 10 mgm. He has devised a long instrument with a revolving barrel attached, whereby ten or more seeds can be inserted without completely withdrawing the instrument.

CANCER TONSILLÆ

Cancer here is of the most malignant type. Practically no five-year reports have been found. The three-year cure rates range between 4 and 10 per cent [Kuettner (62), 7.7 per cent; Burnam (20), 9.75 per cent in 123 cases], with the sole exception of Berven's recent encouraging results at the Radiumhemmet, Stockholm.

Treatment depends wholly on radiation for what results there are. The region is beyond the reach of effective surgery. The tumors are classified, as we have seen, into the adult, resistant squamous-cell carcinoma, the sensitive transitional cell, and lympho-epitheliomas and sarcoma. At the Radiumhemmet (8), till 1924, x-ray plus surface radium were used in 28 cases. Only 25 per cent had primary healing, and all were dead within three years. Since 1924, the cases have been treated with teleradium (the 5 gm. bomb at 6 cm. for 100 to 150 gram-hours through several portals), followed by either surface or interstitial radium, or coagulation of the regressed tumor remnant. Eighteen cases were thus treated, up to 1927, with 7 (or 39 per cent) living more than three years. While deductions should be cautious from series of less than a hundred cases, these results are regarded as the best yet reported.

Burnam (20), Berven (6), Cade (23) and others who have employed both methods are convinced that the effects of mass radiation at a distance (teleradium) are very much superior to those obtained by x-ray. These authors regard this as the greatest recent advance in mouth and pharynx therapy.

Since the disease is so difficult to control, a thorough course of combined radiation should be carried out. Intensive external radiation, preferably by teleradium, should be followed in three to six weeks, with subsidence of the reaction, by interstitial radium. With the adult squamous-cell cancer principal dependence must be placed on the implantation technic. With transitional-cell epithelioma, the combined treatment is best; while with lympho-epithelioma, the intensive teleradiation alone is effective (Burnam). The latter author uses interstitially radon tubes with gold or platinum filter. He uses larger units (2 mgm.) and fewer of them. Heavy implantation is frequently followed by sloughs, which are extremely slow in healing and may give discomfort for months. However, if the growth has disappeared these areas heal and the functional result is good.

Untoward reactions to radiation easily occur. The tonsil is surrounded by radiosensitive normal tissues, leading to injury, pain, and disagreeable symptoms. The salivary glands are injured easily. The periosteum of the mandible and hard palate are very sensitive, and heavy cross-firing can easily destroy large parts of the mandible. Recognizing these hazards, Burnam states, "If radiation is used it should be carried to a dosage beyond that necessary to cause primary regression or disappearance of the tumor." He has seen many patients who have been cross-fired through large portals, front, lateral, and back, followed by intense dryness of the throat, loss of hair, irritation of the skin, with no alteration of the tumor.

Interstitial radium in Harmer and Russell's (51) hands gave palliation but few cures, leading them to the statement that growths in the region of the fauces are almost always incurable. Lang ligates the external carotid artery preventively, then inserts gold-filtered needles (1–2 mgm.) through the mouth and from below the mandible, taking great care not to let the point of the needle come onto the mouth.

This latter error led to fatal sepsis in one case. Of five cases so treated, he obtained primary healing in three.

Much better results are seen with radiation of sarcomas of the tonsil. Striking regression usually results from roentgen treatment alone, after the Coutard technic. Berven (9) supplements this with the surface application of radium. He reports 36.5 per cent five-year cures in the unstated number of cases treated from 1916 to 1927.

In brief, we see that x-ray therapy is reserved for the lympho-epithelioma, sarcoma, and lymphosarcoma groups. For the remainder, the combined therapy of teleradium (or x-ray), interstitial radium, and endothermy is preferred. Surface radium is difficult to apply and to maintain in correct position.

TREATMENT OF CERVICAL NODES

Early treatment of the cervical lymphatic areas in every case is imperative, no matter how effective the primary cure. We have seen that, once metastases have developed in the neck nodes, the chance for cure by any treatment is practically lost. While surgery may cure a few such cases, no cures from any form of external irradiation can be expected. In 72 cases with neck metastases, Forssell (40) obtained no cures by radiation.

Prophylactic treatment of the neck areas, therefore, becomes the all-important factor. Years of experience have shown that prophylactic external irradiation is uncertain, and that it should be used only in combination with surgery (Regaud, 90). Berven,[5] at the Radiumhemmet, administers only a pre-operative dose of teleradium to all cases (50–75 gram-hours total through two portals on each side of the neck), with no attempt to give intense curative dosages.

The majority of radiologists practise the policy of applying external radiation to the neck areas and waiting for further developments (Berven, Cade, Collin, Duffy, Jacoby, Quick, Regaud, Stewart). If nodes develop later, these authors advise dissection, if the cancer has not invaded the capsule of the nodes to cause fixation (inoperability). Does this mean that sight has been lost of the fact that when metastases have developed the chance for cure is practically lost, whether or not the node capsule is invaded?

Evidence that prophylactic radiation of the neck nodes has reduced the frequency of later metastases is difficult to obtain. Regaud, with an eight-gram bomb recently installed (November, 1934), favors teleradium ever more strongly in the effort to supplant prophylactic dissection of the neck areas. This experimental work is, as it should be, confined to the larger centers for investigation.

To serve the best interests of the patient, however, main dependence must, with few exceptions, be placed on early *en bloc* dissection of the neck areas before the nodes are involved. Theories as to the protective function of the lymph nodes [Janeway (56), Quick (87), Berven (5)] cannot justify a waiting policy, depending completely upon the uncertain effect of external radiation, which must not be so intense as to injure the tissues where later operative attack may be necessary. The penalty of waiting is too great. If the nodes become invaded, the chance of cure is precipitously diminished.

One recognizes the protective function of the axillary nodes in breast cancer, yet the marked reduction in the chance of cure, once the axillary nodes are invaded, makes it imperative that they be removed without delay. Too much importance has been attached to the protection rendered by the cervical lymphatics. Answering the question as to why cancer metastases grow so regularly in the lymph nodes, Murphy (79) suggests that the lymphocyte as it exists in the node is inactive, and is capable of functioning only when it migrates into the tissues, just as the polymorphonuclear leukocyte cannot perform one of its important functions, that of phagocytosis, inside the blood vessels—hence, the growth of cancer in the presence of antagonistic cells.

Small, early lesions of the lip, without

ulceration, deep infiltration or nodes, and of low grade malignancy (Grade I) may be given irradiation to the neck areas after the eradication of the primary, and be controlled by careful follow-up examination. All others should have early dissection of at least the submental, submaxillary, and upper deep cervical region on the same side [Eggers (31), Kennedy (58), Lund and Holton (66)]. If the lesion is in the center of the lip, the question of bilateral dissection comes up. Among the 531 cases reported by Broders (18), 76.26 per cent of those operated upon and that showed no metastases were clinically cured. Kennedy (58), in 246 cases treated by surgery both to the primary and to the neck region, obtained 88 per cent cures in cases with the lesion under 3 cm. in diameter and 44 per cent in those over 3 centimeters.

With lesions primary in the tongue, floor of the mouth and mandible, early dissection, after subsidence of the primary reaction, should be carried out wherever feasible, even when palpable nodes are not present [Evans and Cade (33), Fischel (38), Kuettner (62), New and Judd (27), Regaud (91)] until recent adoption of teleradium [Rieder (6), Roux-Berger (97 and 98), Simmons (103)]. Regaud (91), until recent emphasis on teleradium,[5] advised neck dissection in cancer of the mouth in general, usually three weeks after treatment of the primary lesion. If the nodes showed cancer histologically, then post-operative surface radium on wax molds was applied to the neck areas. Berven[6] administers preoperative teleradium, through two portals over the neck areas on each side, at the same time as treatment of the primary. If no nodes are present, he waits until they appear, except in cases of extensive primary lesions. Quick (87) leans most strongly away from surgery, gives external radiation, and exposes and implants radon seeds in nodes as they appear.

Poor general condition, recurrence of the primary lesion, metastasis below the clavicle, fixation to the spinal column, extensive skin invasion, and tumors of embryonal type are regarded as contraindications to operation.

The only adequate removal is the "block dissection," so named and well described by Crile (26), in 1906. He devised this operation in 1898, after the Halstead breast operation. The technic is essentially unchanged to-day. Removal of the sternomastoid muscle and the internal jugular vein should be decided upon in the individual case, especially where involvement of the nodes seems likely. The procedure is simplified by using the plane of interjugulocarotid cleavage, from below upward, dissecting gently with the finger. Roux-Berger and Tailhefer (98-*a*) advise resection of the posterior belly of the digastric muscle and the stylohyoid muscle so as to allow free dissection of the jugular vein up to the base of the skull. They state that the most frequent invasion of nodes from tongue cancer occurs in those behind the angle of the jaw. They have done the above in 23 cases without mishap.

During the dissection, Fraser (44) inserts from 30 to 40 mgm. of radon seeds under the posterior belly of the digastric muscle, for here the dissection is usually incomplete.

The factors determining the extent of the operative attack are well outlined by Jamieson and Dobson (55). Growths on the lateral border of the tongue indicate unilateral bloc dissection, after eradication of the primary. Those of the tip and frenum of the tongue require bilateral dissection, in separate stages. Likewise advanced lesions of the tip, border, and dorsum going over to the alveoli or floor of the mouth, require bilateral dissection. The internal jugular vein should not be sacrificed on both sides. Neck dissection properly carried out should not lead to mutilative disfigurement. Recurrence after adenectomy is low (Roux-Berger and Monod, 98). The experienced technics outlined by Crile (26), Roux-Berger, and Semken are recommended.

With lesions of the cheek, alveolar margin of the upper jaw and palate a more con-

[5] Observed, November, 1934.
[6] Personal communication, 1934.

servative attitude may be taken, based on dissection of the neck on the same side, especially when the primary cancer is extensive.

Lesions of the tonsil and base of the tongue more frequently show an undifferentiated histologic picture, *i.e.*, transitional cell, lympho-epithelioma, or sarcoma. The neck nodes tend to occur as a diffuse ill-defined chain, as opposed to the more localized groups of adult epidermoid metastases. These are best controlled by external radiation, either x-ray or teleradium (Berven, Quick, Regaud). Burnam, however, recommends removing movable nodes in cancer of the tonsil.

Treatment of inoperable, fixed metastases is indisputably by radiation, both external and by implantation of radon seeds. The exposure and implantation of radon seeds in operable nodes as they become involved, proposed by Quick (82), has found but limited acceptance as a substitute for surgery. At the Radiumhemmet, Stockholm, and L'Institute du Radium, Paris, excision is regarded as the most effective treatment.

PROGNOSIS

Limitations should be placed on the importance of grading of tumors as an index to prognosis. MacCarty (68) lists at least seventeen factors which must be considered, namely, the type, size, and location of the lesion, nodal involvement, fixation, renal and cardiac efficiency, anemia, age, duration, direction of growth, weight loss, degree of cellular differentiation, lymphocytic infiltration, fibrosis, hyalinization, and the extent of destruction produced by treatment. Numerical grading deals with but one of these factors, differentiation.

Stewart (110) points out that grading of tumors is not new. Its principles were recognized by Virchow in his "Scala der Malignität" and by a host of others since. It has been popularized of late, with the substitution of figures for complicated pathologic descriptions. Broders classification has shown itself to be of value for group prognosis. It is far too little for individual prognosis, as is seen from the above factors enumerated.

Rieder (93), using Broders' classification in 82 cases of tongue cancer, found no agreement between the clinical results and grading of at least half of the so-called differentiated cases. He states that the subjective element is too great to allow of certain numerical grading. Even with additional data plus the histologic picture, a 30 per cent discrepancy resulted, when compared with the end-results. In these cases recurrence or metastases occurred, although histologically a good result was expected.

SUMMARY

The difficulties attending treatment of intra-oral cancer have been examined. Attempt at comprehensiveness, based on anatomico-pathologic study and a degree of acquaintance with both radiation and surgical treatment of this region, has been made.

CONCLUSIONS

Intra-oral cancer, among the most accessible, remains among the most fatal of malignant diseases.

Since 1910, intra-tumoral radium has played a progressively dominant part in the treatment of cancer of the mouth.

Over 90 per cent of malignant tumors of the mouth are epidermoid carcinomas, mostly of the adult resistant type.

Of the buccal epithelium, the basement cell alone has the power of reproduction and of invasion. All other cell changes represent stages of degeneration.

Epulis, regarded by some as a granuloma, is "semi-malignant."

Leukoplakia is the most important precancerous lesion. All cases of leukoplakia are curable.

Enlarged cervical nodes should be regarded as cancerous. Once cancer invades the cervical nodes the chance for cure is practically lost.

Early diagnosis will improve the results more than any other single factor.

Radium is the treatment of choice of the primary lesion in all cases which have extended beyond the possibility of easy operative removal.

Intratumoral radium must be of epidermicidal intensity, whether over a short or long period, to be reliably effective. In this form it is the best caustic ever devised for cancer.

The 1934 technic of the Radiumhemmet, Stockholm, and L'Institute du Radium, Paris, are presented.

What cures there are in cancer of the tonsil have come from radiation, which must be rigorously employed.

In the treatment of the cervical lymphatic areas, irradiation is uncertain. It should be used only in combination with surgery, which should be early and radical. The penalty of waiting until nodes develop is too great.

Grading of tumors is but one of at least seventeen factors in determining individual prognosis. It is of especial value in determining group prognosis.

Better management of the indivividual case will result from the surgeon and radiologist working together than from either alone.

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ADENOMYOMA OF THE RECTOVAGINAL SEPTUM TREATED WITH RADIOLOGIC METHODS[1]

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THIS study is a review of 36 cases of adenomyoma of the rectovaginal septum, in which the patients were referred to the Section on Therapeutic Radiology, at the Mayo Clinic. The first case was observed in 1918, and the last three cases were observed in 1934.

An adenomyoma is a tumor composed of glandular and muscular tissue. Considered from a general standpoint, this type of tumor may be found in many organs of the body, and when so situated, it usually is representative of the structure of the tissue from which it arises.

This consideration deals in part with adenomyomas of the uterus, and specifically with adenomyomas found in the rectovaginal space. Lockyer, in 1913, presented a paper entitled "Adenomyoma in the Recto-uterine and Recto-vaginal Septa," and he accordingly is accredited with having been the first to identify this phase of the disease. Keene and Kimbrough found that the earliest contribution to the subject, which dealt with adenomyomas of the uterus, was the report by Rokitansky, in 1860. In 1896, the work of von Recklinghausen appeared, and, almost simultaneously, Cullen presented his report of similar tumors that were found in the round ligaments. He is accredited with having been the first to demonstrate that the glandular inclusions in adenomyomas are of endometrial origin. Prior to the work of Sampson, in 1921, this disease was considered a pathologic curiosity and, therefore, of little or no clinical significance. His theories may be questioned, but the value of his work is outstanding.

The theories of origin, which have been advanced by many observers, are of interest. However, it is not within the scope of this presentation to enter at length into this controversy. The wolffian theory, which has been advanced by von Recklinghausen, attributes the source or origin of the glandular elements of adenomyomas to adult remains of the wolffian system. He considered that these masses were "organoid" tumors in which he could trace the component parts of the mesonephron. The presence of these tumors in the pelvis, rectovaginal septum, external genitalia, groin, and distal end of the right round liagment, was considered to be the result of the extension of the gubernaculum ovarii, which originates at the lower pole of the kidney, through the utero-ovarian ligament, and from the uterus to the groin, through the round ligament.

Cullen advanced the mucosal invasion theory because he was able to trace a direct communication between the glandular portion of the tumor and the uterine mucosa. He considered that other tumors, which were similar to those that are found in the uterus, were the result of displaced müllerian rests. Russell is credited with having been the first to report a case in which endometrial tissue was found in the ovary. He assigned its origin to "an aberrant portion of the müllerian duct." Cullen suggested the müllerian rest theory to explain the occurrence of adenomyoma in the right round ligament. The theory is based on the close relationship between the anlage of the ovary and Müller's duct and the possible interchange of cells. Russell said, "It is not hard to conceive that a portion of germinal epithelium which forms the ovary should, at times, attempt to produce structures which its function elsewhere calls upon it to do."

The serosal theory is based on the observations that the endothelial cells of the peritoneum may undergo transformation into cylindric or cuboidal cells, through the

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influence of inflammatory processes, and that the connective tissue in the region of these cellular inclusions undergoes hyperplasia, which may closely resemble the cellular stroma of the uterine mucosa. Meyer is given the credit for demonstrating this theory and describing the pathologic change as a healing process.

The implantation theory of Sampson, which was reported in 1921, rests on the idea that uterine or tubal epithelium may escape through the fallopian tubes into the peritoneal cavity at the time of menstruation, and that when these particles of tissue find lodgment they may penetrate the tissue involved. Sampson has advanced much evidence to support this theory.

These theories are not all-inclusive; however, they stimulated research and discussion, which have advanced our knowledge of this disease. It is necessary to accept the influence of the ovarian hormone on these tumors, as well as their reaction to menstruation and pregnancy. This hormonal feature is very important to the physician who plans to treat this neoplastic disease.

INCIDENCE

The occurrence of adenomyomas (endometriosis) is more common than generally is supposed, and the importance of these tumors evidently has not been recognized. Cullen, in 1908, reported that adenomyoma was present in 83, or 5.7 per cent, of 1,283 cases of fibromyoma of the uterus. In 1919, MacCarty and Blackman reported that adenomyoma was present in 211 of 3,398 cases of fibromyoma of the uterus, an incidence of 6.4 per cent.

Owing to the invasive nature and migratory characteristics of these tumors, many structures of the body may be involved. The following structures have been involved: ovaries, uterus, rectum, sigmoid flexure, round ligaments, broad ligaments, walls of the vagina, inguinal region, external genitalia, walls of the intestine, appendix, bladder, abdominal scars, omentum, fallopian tubes, and peritoneum.

TABLE I.—INCIDENCE OF ADENOMYOMA IN VARIOUS SITUATIONS

Situation	Keene and Kimbrough		King	
	Cases		Cases	
	No.	Per cent	No.	Per cent
Rectovaginal septum	6	5.0	52	42.6
Ovary	110[2]	92.4	23	18.9
Umbilicus and ovary	2	1.7	0	
Laparotomy scar	1	0.8	0	
Peritoneum	0		26	21.3
Uterus	0		17	13.9
Tube	0		4	3.3
Total	119	99.9	122	100.0

[2] Unilateral 63; bilateral 47.

TABLE II.—INCIDENCE OF ADENOMYOMA ACCORDING TO AGE OF PATIENT

Age of patient, years	Cases	
	No.	Per cent
25 to 29	2	5.55
30 to 34	11	30.55
35 to 39	10	27.77
40 to 44	5	13.89
45 to 49	8	22.22
Total	36	99.98

An attempt was made to determine the incidence of adenomyoma of the rectovaginal septum, but neither the reports in the literature nor the material at my disposal lends itself to this estimation. The incidence according to the situation of the involvement, as reported by Keene and Kimbrough, and by King, is given in Table I. In the cases that form the basis of the present study, the patients were referred to the Section of Therapeutic Radiology because of involvement of the rectovaginal space. Therefore, the incidence of involvement of the rectovaginal septum should be rather high in this group of cases, because the situation of the infiltration makes the diagnosis a comparatively simple affair.

Age Incidence.—The age incidence is shown in Table II. Since this disease is influenced by the menstrual cycle and apparently develops slowly, these few cases would seem to indicate that the neoplasm requires at least from ten to twelve years for development, and probably much longer in the older age groups. The time of onset is as yet clinically impossible of determination. It also may be inferred

TABLE III.—MENSTRUAL HISTORY IN 36 CASES OF ADENOMYOMA

	Cases	
	No.	Per cent
Normal and regular	12	33.33
Regular (dysmenorrhea and menorrhagia in five cases)	14	38.88
Irregular	10	27.77
Total	36	99.98

TABLE IV.—CHIEF COMPLAINTS IN CASES OF ADENOMYOMA

	Cases	
	No.	Per cent
Pain in lower part of abdomen	8	22.2
Pain in inguinal region	1	2.8
Pain in buttock	1	2.8
Pain in epigastrium	1	2.8
Pain in rectum	7	19.4
Dysmenorrhea	2	5.6
Menstrual irregularity	5	13.9
Tumor	5	13.9
Carcinoma	2	5.6
Fatigue	2	5.6
Rectal bleeding	1	2.8
Diarrhea	1	2.8
Total	36	100.2

that the cessation of menstruation reduces the number of instances in which the condition is discovered among elderly women. While these cases are too few to permit definite statements, the trend of the disease is shown rather clearly.

GYNECOLOGIC HISTORY

In the 36 cases that form the basis of this study, the gynecologic history was as follows: Ten, or 27.8 per cent, of the patients were single, and 26, or 72.2 per cent, of the patients were married. Seven of the patients had had one child each; two of these patients had had one or more miscarriages. Six patients had had two children each. Two patients had had three children each, and another patient had had four children and two miscarriages. One patient had had six children. Nine of the patients who were married had never had any children or any miscarriages. Adenomyoma may be a factor in the production of sterility, as it may infiltrate the cervix and fix, or limit the motion of, the fundus. The discharge which it produces also may alter the chemistry of the vaginal secretion.

The menstrual history is of great assistance in establishing the diagnosis, because the symptoms may be associated with or aggravated by the menstrual cycle. The menstrual history in these cases is recorded briefly in Table III. Many of the phenomena of disturbed menstruation depend on the extent and situation of the lesion. The presence or absence of surface ulceration is a factor. The menstrual discomfort is of the acquired type. There is a possibility that this association may have been overlooked in the cases which were seen first.

Vicarious menstruation was noted in nine, or 25 per cent, of the cases. In eight of these cases, there was blood in the stool at the time of menstruation. This establishes the importance of a rectal examination by endoscopic methods in these cases. In one case there was a bloody discharge from the navel.

Dyspareunia was recorded in four of the cases (11 per cent). This feature depends chiefly on the extent of involvement and fixation of the pelvic structures. The incidence may be higher than it appears, as this information seldom is volunteered by the patient.

CHIEF COMPLAINTS

The major chief complaints are recorded in Table IV. Many patients had multiple complaints, some of which were referable to the disease, while others were unrelated to the adenomyoma. An attempt was made to group these complaints according to the importance that the patient placed on them.

In 20 cases (55 per cent), pain was the chief symptom. In eight of these, the pain was situated in the lower part of the abdomen, and in seven, it was situated in the rectum. Seven patients (19.5 per cent) complained of menstrual disturbances. In seven cases (19.5 per cent), the patients complained of a tumor, or of a carcinoma; in these, the diagnosis usually had been made by the attending physician. The chief symptom was related to or modified by menstruation in 20 cases (55.5 per cent).

In 16 cases (44.4 per cent) the history did not reveal any relation between the chief symptom and menstruation. This figure probably is unreliable, as the relation between the chief symptom and menstruation can be established in a very large number of these cases, if this condition is suspected. It may require careful questioning to elicit this relationship. Adenomyoma should be suspected in all cases in which this relationship can be demonstrated.

The duration of the signs and symptoms is recorded in Table V. Evidently, the development of these growths may be considered slow or moderately slow, especially when the size of the neoplasm and the duration of the chief symptom are considered. As a rule, these growths are not large or bulk infiltrations, such as commonly are seen in cases with a lengthy history in which malignant disease is present. This disproportion should also awaken the thought or idea that the disease may be an adenomyoma.

TABLE V.—DURATION OF SYMPTOMS OF ADENOMYOMA

Years[3]	Cases	
	No.	Per cent
Less than 1	12	33.33
1 to 2	10	27.77
2 to 3	5	13.89
3 to 4	2	5.55
4 to 5	1	2.77
5 to 6	3	8.33
8 to 9	2	5.55
9 to 10	1	2.77
Total	36	99.96

[3] Longest duration, 9 years; shortest duration, 6 weeks.

TABLE VI.—GYNECOLOGIC AND CLINICAL DIAGNOSIS

Diagnosis	Cases	
	No.	Per cent
Adenomyoma	26	72.22
Carcinoma	5	13.89
Tumor	5	13.89
Total	36	100.00

GYNECOLOGIC AND CLINICAL DIAGNOSIS

The diagnosis usually can be made as a result of bimanual pelvic examination and careful inspection of the vaginal mucosa. The infiltration usually is described as a nodular or multinodular mass that is situated in the region of the vaginal *cul de sac*. The mass may extend anteriorly to the posterior wall of the vagina, or laterally to the right or left fornix of the vagina. In cases in which the growth is situated in this region, it becomes attached to, or involves, the neighboring structures, especially the anterior wall of the rectum and the vaginal wall in the region of the *cul de sac*. Tenderness may or may not be present during palpation. The extension laterally may infiltrate the broad ligament and result in a large fixed mass in the pelvis. There may be slight or moderate obstruction of the rectum. In some cases the rectal obstruction may be so severe as to necessitate a colostomy. The ureters may be included in the pelvic mass, and a unilateral or bilateral hydronephrosis may result. In some of the cases, the walls of the urinary bladder were involved. The growth may infiltrate the cervix, especially the supravaginal portion, and the posterior wall of the fundus of the uterus. Various physicians have reported involvement of the external genitalia, inguinal region, abdominal scars, and umbilicus. An exploratory laparotomy may reveal the characteristic tumors and dense adhesions of the pelvic structures. Involvement of the ovaries, rectum, rectosigmoid, sigmoid flexure, omentum, broad ligaments, and round ligaments has been reported. In cases in which there is an adhesion of the epithelial tissue which covers these tumors, there is a bluish discoloration of the tumors. The discharge, which occurs in cases in which the tumor is broken or undergoes ulceration, is similar to the menstrual discharge, and its occurrence always has some relation to the menstrual cycle. In 14 of the cases in this series, the tumor was small; in two cases, it was large, and in the rest of the cases, the size of the tumor was not mentioned. In the 14 cases in which the tumors were small, the average size of the growth was 3.6 by 4.2 centimeters. The smallest

TABLE VII.—CLASSIFICATION ACCORDING TO CULLEN

	Cases	
	No.	Per cent
Group 1	2	5.55
Group 2	11	30.55
Group 3	11	30.55
Group 4	12	33.33
Total	36	99.98

tumor measured 0.5 by 0.5 cm., and the largest tumor measured 5 by 6 centimeters. In 14 cases, the growth was fixed or adherent to adjacent structures. Retroversion of the uterus was noted in ten cases, which was a rather high incidence. In cases in which there are extensive infiltrations, the uterus is intimately associated with the pelvic infiltration, and it is impossible to be certain regarding the size and situation of the fundus of the uterus. The rugæ of the vagina persist, and there may be sessile polypoid masses, or definite pedunculate polyps in the vagina in some cases. The latter feature lends weight to the inflammatory theory of the origin of this neoplastic disease.

The tentative diagnosis, which was made at the time these patients first registered at the Clinic, is given in Table VI. The cautious diagnoses of tumor and of carcinoma were made in the early years of this study. A careful history, palpation, and inspection should reveal the correct diagnosis. Biopsy may be performed to substantiate the diagnosis, especially in cases in which there are denuded or ulcerated lesions in the vaginal *cul de sac*.

PROCTOSCOPIC EXAMINATION

The general physical condition of these patients is very good and no definite undermining of their health was noted. Aside from the usual laboratory tests, no special tests are indicated. The most common special examination which was done was a proctoscopic one. Miles, in 1921, pointed out the significance of this disease entity in the field of proctology. On account of the situation of the infiltration between the rectum and vagina, and because of the likelihood of involvement of the anterior rectal wall, rectal distress may be the chief symptom.

In 18 cases (50 per cent), a proctoscopic examination was done. This revealed positive findings in 14 cases (77.77 per cent) and negative findings in four (22.22 per cent). The most common proctoscopic finding was an extra-rectal mass, which occurred in 12 cases, and was situated about 10 cm. from the anus, involving chiefly the anterior wall of the rectum. The rectal mucosa may be attached or adherent to the surface of the infiltration; it may bleed easily when touched, or ulceration may be present. The mass may encroach on the lumen of the intestine and produce a mild or severe rectal obstruction. In all but two of the cases in which a diagnosis of a malignant or doubtfully malignant lesion was made by the proctologist, the report was only a description of the findings and was not a proctoscopic diagnosis. Patients who have definite rectal symptoms should be subjected to a proctoscopic examination. It should be a consideration in all cases to rule out the possibility of involvement of the rectum. The proctologist must be alert to recognize this disease entity.

CLASSIFICATION OF CASES

Cullen, in 1917, suggested the following classification for a similar group of cases: *Group 1.* Small tumor, single or multiple, is relatively free in rectovaginal septum. *Group 2.* Tumor is adherent to posterior surface of cervix and anterior surface of rectum. *Group 3.* Tumor glues cervix and rectum together, and spreads into one or both broad ligaments; tumor is not fixed. *Group 4.* Tumor involves posterior surface of cervix, rectum, and broad ligament. There is a diffuse pelvic mass which is fixed and causes partial obstruction (rectum, ureters).

An attempt was made to classify the 36 cases in this manner, by employing the data contained in the history, surgical cards, and records of special examinations. The results of this classification are shown in Table VII.

GROSS AND MICROSCOPIC PATHOLOGY

Mahle and MacCarty have described the adenomyomas of the rectovaginal septum as follows:

"Pathologically, extra-uterine adenomyomas are identical in appearance regardless of where they are found. They differ grossly from adenomyoma of the uterus, in that the cystic areas are larger and the contents darker brown. Grossly, the tumors are solid, fibrous, and of a light gray color. Here and there, white bands extend into the tumor substance, while between these bands are areas, dark brown to almost black, varying in size from the head of a pin to cystic areas 1 cm. or more in diameter.

"Microscopically, the stroma consists of fibrous connective tissue and smooth muscle fibers, the latter in varying amounts. Within the stroma are gland spaces lined with cylindrical epithelium. Some glands are surrounded by a very cellular stroma, the cells of which are regular with round or oval nuclei resting in a very fine reticulum, while other glands are immediately surrounded by smooth muscle or connective tissue. In some portions of the tumor substance there is marked evidence of recent and old hemorrhage. In the latter areas are clumps of endothelial cells filled with old blood pigment, and in one of these areas a typical foreign body giant cell is seen enclosing a mass of blood pigment. The adenomatous portions of these tumors with their cellular stroma are identical with uterine endometrium.

"Clinically, these tumors give no consistant group of symptoms on which an accurate diagnosis can be made. However, their location and slow growth, extending over a period of years, suggest benign tumors. Further, the occasional relation to the time of menstruation, of pain or swelling of the tumor, or less frequently a bloody discharge should be very suggestive of adenomyoma.

"Surgically, adenomyomas, regardless of their remarkable infiltration characteristics, should be differentiated from malignancy. Especially is this true of the tumors in the pelvis, adherent to the sigmoid or the abdominal wall, or other structures. Adenomyomas may be recognized grossly in most cases by the fibrous stroma which contains cystic areas filled with a bloody, dark brown, or serous fluid.

"The pathologist should distinguish adenomyoma from carcinoma by the regularity of gland structure with normal differentiated epithelial cells without mitosis and, in most tumors, by the characteristic stroma surrounding the glands. He should also recognize that they are benign tumors, that they grow by invasion, and do not metastasize."

TREATMENT AND RESULTS

Keene and Kimbrough stressed the acceptance of the fact that the activity and proliferation of these tumors are dependent on ovarian function, and, conversely, that ablation of ovarian function will cause these tumors to atrophy. Therefore, the surgeon and radiotherapeutist must be guided accordingly in the treatment of this disease. Since the disease affects women who are comparatively young, the problem is not always a simple one, and it usually is wise to err on the side of conservatism.

Adenomyomas which cause rectal pain, bleeding, and backache, can be treated with radium and roentgen rays, but the desired results require a menopausal dose. Graves (4, 5) pointed out that regression does not always occur with cessation of the menstrual cycle, assuming that these patients have passed the bound of this hormone influence. Apparently none of the patients in these cases could be so classed. Sampson and others have demonstrated that these lesions may undergo malignant degeneration. These tumors are composed of endometrial tissue and therefore are subject to malignant change. There was no certain evidence of the malignant phenomena in this series of cases. Although the possibility or probability of malignant change is evidently very small, it must be reckoned with.

The management of the cases seen in the early years of the recognition of this disease entity was "entirely operative." Operation was the first and only method of treatment, and deserves much credit for advancing our knowledge of this "devastating and fatal" disease. Surgical material furnished much valuable information, which shortened the time necessary for a correct diagnosis and the institution of effective therapy. To-day, surgical interference is the treatment of choice in certain forms of this disease, for example, in cases in which there is ovarian involvement. In other cases surgical removal is most difficult, and in some cases it is impossible. One of the characteristics of the disease is to form

firm dense fusion of neighboring structures, which makes their separation difficult, and in some cases impossible.

It is not within the scope of this paper to discuss at length the operations which are employed in these cases. However, it is important for the radiotherapeutist to know what type of surgical procedure was done, in order to outline adequate irradiation therapy.

Seventeen of the patients had submitted to some type of pelvic operation for this disease before they came to the Clinic. Eight of these operations could be classed as radical, while nine were conservative. These consisted of local excision, removal of specimen, some type of cautery, and so forth. In one case in which a radical operation had been performed elsewhere, a recto-vaginal fistula had developed shortly after the operation. In 24 of the cases in which operation was performed at the Clinic, some type of conservative procedure was done. In two of the cases, the operation was radical, and in ten cases, the condition was not treated operatively at the Clinic. There was one death in the hospital, caused by peritonitis. An exploratory laparotomy was performed in seven cases. In one of these cases there was one tumor, in another case there were two tumors, and in a third case there were three tumors. In one case there was an extensive infiltrating tumor in the vaginal *cul de sac*, which involved the rectum, the cervix, and the anterior wall of the rectosigmoid. Separation was considered dangerous, and a loop colostomy was all that was done.

From the standpoint of irradiation therapy, the cases may be classed in two groups: (1) those in which the treatment was directed toward the local infiltration as a primary malignant neoplasm, and (2) those in which the treatment was given to control menstruation, and thus indirectly to influence the neoplastic process. There were 15 cases (41.7 per cent) in which the treatment was direct, and 21 cases (58.3 per cent) in which the treatment was indirect. The patients who comprise the first group were treated early in our experience, which accounts for the relatively large number of cases in this group. The technic of irradiation consisted chiefly of the application of filtered radium, at various distances, to the vaginal surface of the infiltration, with or without supplemental so-called low voltage roentgen therapy through anterior and posterior pelvic fields. In 1926, the first patients were treated with the indirect method. This technic is intended primarily to control menstruation. In some cases, the intrauterine application of radium, similar to that which is employed in the treatment of menorrhagia with or without fibroids, is used. Radium packs were applied to the vagina. The applicator is the one used in

TABLE VIII.—TYPE OF TREATMENT AND RESULTS

Type of treatment	Cases	Per cent	Deaths in hospital	Good result	Temporary relief	Failure	Indeterminate
Radium (direct)	6	16.66	1	2	2	0	1
Radium (indirect)	8	22.22	0	5	0	1	2
Radium (direct) and roentgen rays	3	8.33	0	2	1[4]	0	0
Radium (indirect) and roentgen rays	9	25.00	0	7	1	0	1
Operation and radium (direct)	2	5.55	0	1	0	1	0
Operation and radium (indirect)	3	8.33	0	2	0	0	1
Operation, radium (direct), and roentgen rays	2	5.55	0	1	1	0	0
Operation, radium (indirect), and roentgen rays	1	2.77	0	1	0	0	0
Radium (indirect at the Clinic; direct elsewhere) and roentgen rays	1	2.77	0	1	0	0	0
Operation only; radium treatment refused	1	2.77	0	0	0	0	1
Total	36		1	22	5	2	6

[4] Died subsequently, cause not known.

the treatment of cervical carcinoma (2). In some cases, the preceding treatment is supplemented with the application of radium packs to the abdominal wall, in the right and left ovarian areas, or with a combination of moderate and high voltage roentgen therapy, as employed in the treatment of menorrhagia (1). A rather wide choice of methods is available in treating this disease.

The type of treatment which was employed in these cases and the results are shown in Table VIII. The incidence of good results in the cases in which the patient was treated by the direct method may be attributed to the fact that the treatment was sufficient to control menstruation. With the return of menstruation, the result was listed as temporary relief since the cessation of menstruation is essential to control the disease. In two cases in which failure resulted, the patients were treated inadequately. One of these was a young woman, aged 25 years, who received an intra-uterine application of 250 millicurie-hours of radium. Later, during the periods of temporary amenorrhea, there was some relief, but she continued to have pain with and without menstruation. In the second case the radium therapy was given in part and then abandoned. A letter from the patient reports that she has had two normal pregnancies and that the growth has disappeared. However, she continues to have pain in the rectum.

The death, which occurred in the hospital, was a case in which the radium treatment was applied before the operation, therefore, it may be considered an operative death.

The indeterminate group is made up of cases in which the patients replied to letters of inquiry but failed to mention their menstrual history. As the control of menstruation is the criteria for good results, these reports were considered incomplete. They were in the main favorable, and the patients evidently were definitely improved or obtained a good result. One patient died four years after the treatment. In this case, amenorrhea had been present for four years; this was followed by vaginal bleeding, which was associated with severe backache. The data are incomplete, so the primary cause of death is unknown. There was no definite information available in this study of the results of treatment which would indicate that malignant degeneration had occurred in an adenomyoma of the rectovaginal septum; however, it must be kept in mind as a possibility.

SUMMARY

In radiotherapy of adenomyoma of the rectovaginal septum, it is necessary to treat ectopic endometrial tissue which has a histologic structure identical with that of the uterine mucosa. Therefore, this tissue is influenced by the ovarian hormone.

The history and physical findings should indicate the diagnosis. Tissue may be removed for biopsy. Every infiltrating tumor in the wall of the posterior vaginal *cul de sac* or in a corresponding region in the anterior rectal wall should not be regarded as malignant. When the infiltration is atypical, an effort should be made to obtain a satisfactory history, for in the average case the symptoms and signs will be influenced by the menstrual cycle.

An effective method of treatment is a therapeutic menopause which is induced with radiation therapy; this is an indirect attack. In the management of young patients (before the age of 35 years) who are seen early, the neoplasm may be removed (1) surgically, or the patient may be observed for some time. Bimanual pelvic examination should be performed every four to six months to determine any change in the neoplasm. This delay should not prove serious as definite malignant degeneration was not proved in any of the cases studied. (2) A trial treatment should be considered to determine possible beneficial effect of a temporary amenorrhea for at least six months to one year. (3) The last consideration should be the induction of a permanent therapeutic menopause with radiation.

In the cases in which the lesion is advanced, there is no choice. The induction

of a therapeutic menopause with radiation is recommended because it favorably influences this destructive neoplastic process. In the cases in which there is rather severe intestinal obstruction a colostomy may be considered, but it should not be performed until the pelvic infiltration has been reduced by indirect irradiation, because it is possible to overcome this serious complication. Mild catharsis, low enemas, and a diet which has little or no residue should be prescribed for a time following the radiation therapy.

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A COMPARISON PHOTOMETER AND ITS USE IN DETERMINING THE DISTRIBUTION OF RADIATION IN A PHANTOM[1]

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A COMBINATION of the ionization and photographic methods was used in determining the distribution of roentgen radiation in a rice phantom. The relative intensities in a central beam of radiation were determined with a small ionization chamber. Other points of equal relative intensity in a cross-sectional area containing the central beam were determined by the use of photographic film. To determine very small areas of equal density on the photographic film it was necessary to use a photometer. The photometer which was built for this work can be used for any photometric work for which the desired data can be obtained by matching the transparencies of two similar objects.

THE PHOTOMETER

One of the difficulties encountered in photometric work is the obtaining of a constant source of illumination. Generally the lamp current is kept constant by the use of a constant wattage transformer or by manual adjustment of a rheostat. The photometer described here was made independent of fluctuations in the intensity of the lamp by the use of two photo-electric cells.

The cells, which were taken from photographic light meters, are similar to the Weston Photronic cells. Each cell is enclosed in a box, so that the only light which falls on the sensitive surfaces enters through small apertures from 1 to 2 mm. in diameter. The boxes containing the cells are so mounted on a frame that the apertures are equidistant from an ordinary electric light bulb (Fig. 1). Lenses from small pocket flashlights are so mounted that a part of the image of the filament of the lamp is focused on the apertures. The two cells, a galvanometer, and a switch are connected in series so that the potentials

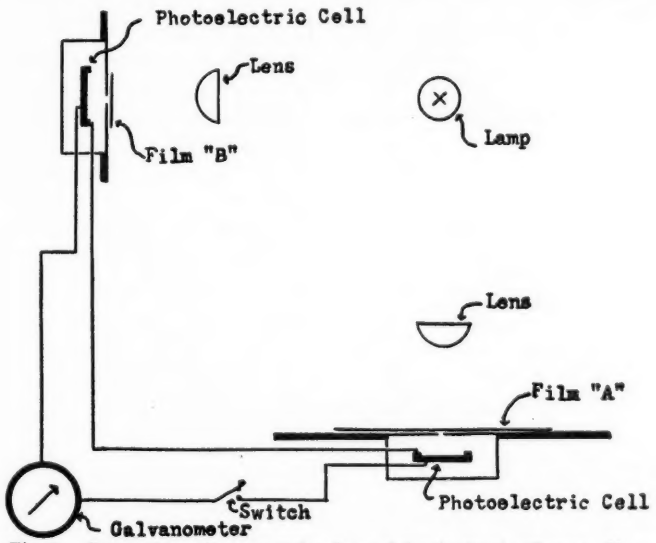

Fig. 1. Comparison photometer for determining isodensity lines on film.

[1] Submitted for publication in December, 1934.

generated in the two cells oppose each other.

No current will flow through the galvanometer when the potentials generated in the two cells are equal. The two potentials will be equal when the cells are equally illuminated. Equal illumination of the two cells can be obtained by adjustment of the light-absorbing materials in front of the two apertures, and the cells will continue to be equally illuminated regardless of fluctuations in the intensity of the light emitted by the lamp.

The instrument as described has been entirely satisfactory for the work for which it has been used; however, its sensitivity and accuracy could be increased by the use of a better lens system and a smaller filament lamp.

DISTRIBUTION OF RADIATION IN A PHANTOM

The intensity in the central beam of radiation in a rice phantom is determined at several depths with a small ionization chamber. From these measurements a graph is drawn, so that the intensity in the central beam of radiation in the phantom can be determined for all depths.

Process film, which has a slow emulsion with a high degree of contrast, is placed between two thin pieces of cardboard bound together around the edges with strips of black gummed paper. The film in its cardboard holder is then placed perpendicularly in the phantom so that it passes through the center of the field to be irradiated. The film is exposed for from 1 to 20 seconds, depending on the intensity of the radiation and the part of the film to be used, and is then carefully developed. A long exposure is necessary to produce a perceptible darkening near the bottom of a film; but, since a long exposure causes the top of the film to be too dark for accurate measurements, it is desirable to expose two or three films for different lengths of time.

From the graph constructed from the ionization measurements, definite values for the relative intensity of the radiation in the phantom can be assigned to the various degrees of density in the midline of the film. Lines of equal density on both sides of the midline are determined by the use of the photometer just described. The film is placed in the position of film "A" in Figure 1. Film "B," a strip of film similar to "A," is used for adjusting the photometer for any desired density in the midline of film "A."

Except for variations in density caused by unequal development, by variations in the thickness of the emulsion of the film, and by the variation in sensitivity of the film to radiation of different qualities, the isodensity lines represent isointensity lines of the radiation in the cross-section of the phantom in which the film was exposed. The positions of the lines traced from films exposed and developed at different times have been found to be very nearly the same. This indicates that variations in density caused by unequal development can be made quite small if reasonable care is used in the development of the films, and that the variations in thickness of the emulsion do not produce appreciable errors. The variation of sensitivity of the film to radiation of different qualities is not an important factor because of the small variations in the quality of the radiation which occur in regions of similar radiation intensity.

Sets of isointensity charts for convenient use can be made by drawing the lines on sheets of white paper, photographing the drawing, and making positive prints on film.

THE EFFECT OF HARD ROENTGEN RAYS AND GAMMA RAYS OF RADIUM[1]

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ONE of the principal points of contention in modern radiobiology is the question as to whether in the domain of roentgen and gamma rays the effect is dependent on the wave length; or, in other words, whether by equal quantities of absorbed energy different wave lengths have a different effect.

For the rays mostly used in therapy emitted at 50 K.V. without filter to 200 K.V. with 2 mm. copper filter, it is generally admitted that there is no marked difference in effect; but especially in respect of the extremely short waves—shorter than 0.1 Å.—our knowledge is still somewhat incomplete and there are great controversies between various authors.

The literature, extensive regarding rays emitted at a tension below 200 K.V., is comparatively scanty for the shorter wave lengths. I shall deal with the literature in broad outline only; completeness not being attainable within the scope of this work, I shall chiefly confine myself to the publications concerning the above-mentioned domain of short waves with which I have met during late years. Among the supporters of the idea of equal effect by the same ionization are:

Holthusen and collaborators, who have principally experimented on *Ascaris* eggs and on the human skin;
Wood, who has made experiments with inoculations of tumor;
Arntzen and Krebs, irradiating seeds of plants;
Alberti, investigating cornea epithelium of salamanders;
Jacobi (lethal dose for mice);
Fricke, Petersen, and Morse (chemical and colloidal reactions);
Rothstein (trypsine reaction);
Piepenborn (lymph glands);
Vierheller and Saralegui (seeds);
Packard (*Drosophila* eggs);
Glocker and his collaborators (chemical and biological experiments);
Schubert (chick embryo);
Groedel and Schneider (yeast and paramecium);
Simon (*Drosophila* eggs);
Regaud (testicles);
Hess, Grebe and Martius, Sievert, Klein and Gaertner, all of whom have examined the reaction of the human skin.

A smaller but still important number of researchers hold the opinion that soft rays have a stronger effect, several of them having investigated the reaction of the skin. Among these are numbered:

Wintz and Rump, Glasser and his collaborators, Jona, Stahel, Murdock and Simon, whilst many have made use of other objects.
Strangeways and Hopwood (tissue-cultures);
Crowther (protozoa);
Russ and Scott (tumor);
Gunsett, Ancel, and Spack (lentils);
Schugt (castration of mice);
Holweck and Lacassagne (bacteria, yeast, and protozoa).

Adherents of the opinion that hard rays have a greater effect are much fewer in number. I may mention among others: Bolaffio, Reinhard, and Zuppinger, working in the field of biology as well as of chemistry. There are also researchers who believe that there is no definite linear dependency of the effect on the wave length, but that special wave lengths are particularly effective (Dognon and Failla).

Apart from these opinions concerning the quantitative proportions, a few other authors believe a qualitative different action of different wave lengths to be demon-

[1] Read before the Fourth International Congress of Radiology, Zurich, July, 1934.

strable, *e.g.*, Vohwinkel, who examined germinating lentils. Moreover, some authors admit a so-called "differential action," by which they understand the alternation of the proportions of sensitivity of different tissues when using other qualities. Thus Russ and Scott describe the diminution of the ratio:

$$\frac{\text{lethal effect on tumor}}{\text{permanent complete depilation of the skin (rat)}}$$

with decreasing wave length. They found that both effects required a greater dose of hard rays, but the relation alters in favor of the tumor dose; consequently the hard rays act in a measure more electively on tumor tissue. Though this opinion has met with opposition from several sides, some account will have to be taken of it, especially since Failla and his co-workers support a similar idea in their recent researches.

This summary shows that there is by no means unanimity, and though the majority of researchers think that by equal ionization or equal absorbed energy, respectively, no varying effect of different wave lengths is to be proved, we might state that other conceptions find numerous prominent supporters. I wish to observe that more or less critical comment is possible upon most of the researches, while much work is already obsolete. Moreover, the number of experiments in the field of radiation with wave lengths below 0.1 Å. is still very small. All these considerations have encouraged me to make a contribution to the solution of this important problem.

In the first place I used roentgen rays produced at 200 K.V. constant potential (Stabilivolt Tuto apparatus) filtered by 1.5 mm. Ag + 2 mm. Cu + 0.5 mm. Al, so that a narrow spectral range of from 0.06 to 0.12 Å. with the maximum intensity at 0.08 Å. and an average wave length at 0.08 Å. is obtained. The spectrum was photographed with a Seemann spectrograph. The silver filter was chosen to eliminate the Wolfram lines and surrounding wave lengths, whilst the copper filter absorbed the silver radiation and the aluminium filtered away the copper rays. The firm of Philips, of Eindhoven, allowed me to work in their laboratory with roentgen rays produced at 360 K.V. (apparatus according to the Witka principle), with Philips Metalix tube filtered by the wall of the tube (3 mm. chrome steel) + 2 mm. tin + 1 mm. Cu + 2 mm. Al. The spectrum of this radiation was not photographed. The quality of radiation was determined by the half value layer in lead which proved to be 0.65 millimeter. Lastly the effect of γ-rays of radium, filtered by 0.5 mm. Fe + 1 mm. Pb, was examined. For comparative purposes I used x-rays emitted at from 100 to 110 K.V. filtered by 0.5 mm. or 1 mm. Cu + 1 mm. Al, taking the effect of this as the unit, and admitting that below 200 K.V. no appreciable differences in effect were noticeable.

MEASUREMENTS

In order to determine the quality of the radiations, I used the method of the half value layer in copper or lead, and for some radiations the spectrophical method. Both methods are sufficiently well known so that I need not enlarge upon them and can refer to Table I.

For intensity or quantity measurements, respectively, a large Siemens dosimeter was employed, which was standardized by a self-made standard chamber built according to the principles of Küstner. On comparing this standard chamber with the apparatus of the Phys. Techn. Reichsan-

TABLE I

Voltage	Filter	Spectrum in Å.	γ Average in Å.	Half value layer in mm.
100 K.V.	0.5 Cu to 1 Cu	0.12–0.4	0.22 or 0.2	0.41 or 0.55 Cu
200 K.V.	1.5 Ag + 2 Cu + 0.5 Al	0.06–0.12	0.08	3.2 Cu
360 K.V.	3 chrome-iron + 2 Sn + 1 Cu + 2 Al	0.034—	0.055	4.6 Cu (0.65 Pb)
Radium	0.5 Fe + 1 Pb	0.0087–0.035		

stalt at Berlin it was found to agree within some percentage.

The dimensions of the cylindrical ionization chamber were 32 × 24 centimeters. The wall is put on high tension and the collector electrode, connected with an electrometer, consists of a eccentrically placed carbon rod. The scale of the Siemens dosimeter appeared to be quite right for the 100 K.V. roentgen rays, but for the 200 K.V. roentgen rays the apparatus was too sensitive, so that a correction of 12.5 per cent was necessary. For the 360 K.V. I was not able to build a standard ionization chamber. The scale of the Siemens dosimeter, wanting already a correction of 12.5 per cent at 200 K.V., was supposed to indicate at 360 K.V., 20 per cent above the exact figure. Neither was I able to perform standardizing measurements for γ-rays of radium. For these measurements I used the Siemens dosimeter with an arbitrary correction of 35 per cent, chosen in connection with the above-mentioned deviation of the scale at 200 K.V.

Since for the γ-ray measurements a special method, differing from the universal ones, was used, I shall describe my procedure. At the time of the commencement of these researches, there was great uncertainty in the matter of γ-ray dosage. Even nowadays the results of the experiments are far from identical; nevertheless, during recent years interesting work has been done on the subject of radium dosimetry. As in the meantime I had to find out my own way to experiment, I chose an approximate solution based on the following ideas.

To begin with, I wish to report that for biological experiments, I used a radium applicator in the shape of a small table, the top of which consisted of lead 1 mm. in thickness, with 1 cm. wooden legs. Upon this table-top fourteen small tubes, of 10 mgr. radium each, were placed in such a way that the intensity on the basis in a central region of about 2.5 cm. diameter was homogeneous, which was controlled photometrically. (See Figure 1, page 60.) According to the law of squares, the intensity upon the base can be calculated, provided the number of r equaling 1 mgr.-/cm. be known. Table II shows the numbers as stated by a few writers.

TABLE II

	Number of r corresponding to 1 mgr.-hr./cm.	
Jona	6.5	Average 5.85
Stahel	7.5	
Neeff	2.8	
Glasser and Mantz	7.4	
Failla	2.2	
Mayneord	8.7	

According to later investigations this average number is on the low side, but may be taken fairly low in our case, as the γ-ray sources in the tubes are not point-shaped, so that the accepted distances represent minimum values. The discrepancy in the numbers of the different authors may be partly explained in this manner. Moreover, the greater path followed through the lead by the slanting line of the rays is not taken into account. This correction, however, effective in the same direction, would be but slight. Thus, taking the average 5.8 r, one arrives at the following approximate calculation:

For the tubes A and A_1

$$\frac{2 \times 30 \times 5.8}{1 + (1.7)^2} = 88 \text{ r per hour}$$

the tubes C and C_1

$$\frac{2 \times 30 \times 5.8}{1 + 1} = 173 \text{ r per hour}$$

the tubes D and D_1

$$\frac{2 \times 10 \times 5.8}{1 + (0.3)^2} = 114 \text{ r per hour}$$

For the whole applicator 375 r per hour = ± 6 r per minute.

(See Figure 2, page 61, and Figure 3, page 62.)

In order to obtain an idea of this intensity for myself, I proceeded as follows: In a 15 × 10 × 5 cm. case built of little leaden blocks, I introduced the ionization chamber of the Siemens dosimeter. At a distance of 7 cm. from this chamber there was on each side a γ-ray source with 70 mgr. of radium. (See Figure 4, page 63.)

The chamber was covered by a wooden layer 1 cm. thick, and between this wood and the chamber I placed a photographic

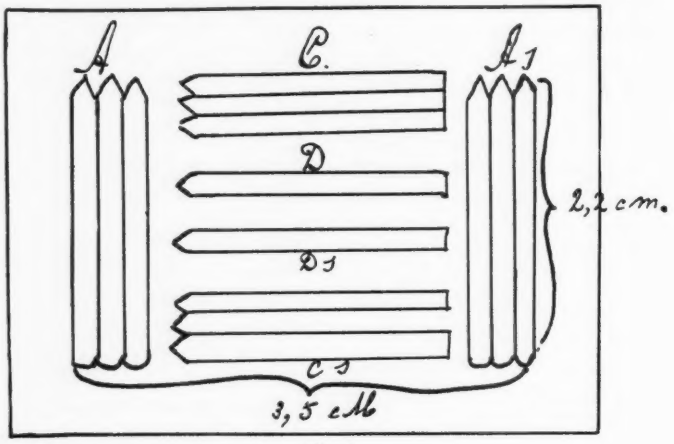


Fig. 1.

film on each side. By sheltering the electrometer and conductor tubes of the dosimeter with 15 cm. of lead, leakage, if any, by radiation was excluded, as was proved by controlling experiments.

The blocks of wood served to avoid the so-called "*Schatteneffekt*," described by Holthusen and Haman. They explain this effect in the following manner: If a metal, *in casu* the lead filter, be irradiated with γ-rays, the secondary β-rays are emitted, especially in a forward direction and, accordingly, they will not decrease with the square of the distance. A much-too-high dose would be measured in that case. If, however, these β-rays are screened off, which is done in our case by the wooden blocks, then this source of error will be neutralized. It is true, the wooden blocks will emit γ-rays again, but their intensity will be parallel to the intensity of γ-rays on that spot. Thus I obtained a blackening of the photographic film, while during the exposure a certain discharge of the electrometer was observed. By switching off a capacity, this electrometer was so sensitive that one could easily read some r. In this manner a certain proportion was found between blackening and ionization. This proportion may be used to calculate the intensity of the table-shaped applicator. For this purpose we exposed a piece of the same film to this applicator for some seconds and then we ascertained the blackening, which can be converted into r by means of the proportion found.

From Table III the results of such an experiment will be seen. (The correction for the developmental fog has been already applied.)

TABLE III

	Film No.	Exposure in seconds	Blackening	
Direct irradiation with table-shaped applicator with 140 mgr. radium	1	20	0.42	
Irradiation with radium at 7 cm.	2	360	0.38	Average 0.40
	3	360	0.41	

The blackening of Films 2 and 3 can be arrived at with an exposure of 19 seconds according to the table. In these 360 seconds the electrometer had run 36 scale divisions, 7 of which must be ascribed to leakage of its own. These 29 divisions corresponded to 1.9 r. So 1.9 r produced a blackening attained in 19 seconds by means of the table-shaped applicator; consequently this applicator gives 6 r per minute, a num-

ber agreeing remarkably well with the calculated intensity. Admitting a correction of 35 per cent for wave length dependency,

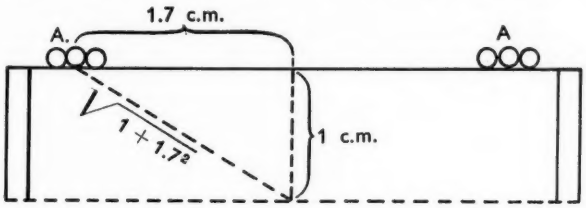


Fig. 2.

we should arrive at 4.5 r per minute. From these numbers we can at the same time get an idea of the number of r corresponding with 1 milligram-hour/centimeter: 140 mgr. at 7 cm. distance gives in 6 min. 1.9 r: that is, 1 mgr. at 1 cm. in one hour

$$\frac{1.9 \times 49 \times 10}{140} = 6.65 \text{ r.}$$

If, however, we have to make the same correction for wave length dependency, we get 5 r, which corresponds fairly to the average value stated in literature.

As to the above-mentioned results, we must consider that the radiation source in this case is not point-shaped, and though at this great distance of 7 cm. no important correction will be necessary, our number will represent a minimum value. In this way, I have succeeded in a measure in expressing the intensities and dosage of γ-rays in roentgens.

MATERIAL

On account of the possibility of the differential effect dealt with in the literature, I have not restricted myself to the investigation of one reaction, but have included several objects in my research. The number of biological, chemical and other objects already used for experiments is legion. My brief mention of the literature gives but a slight idea of it.

The choice seems to be ample enough, yet if higher demands be made on the test-objects, it becomes much more restricted. Referring to the publication of Zuppinger, I would formulate the following conditions for an ideal biological test-object:

(1) The object must be radiosensitive.
(2) The results will have to be easily determined (the criterion must leave no doubt).
(3) The reaction must be fairly exact; in other words, a difference in reaction must be seen at slight differences in dosage.
(4) A comparatively large number of test-objects must be available.
(5) The material must be homogeneous in respect to genotypical purity and state of development.
(6) The reaction must be constant.
(7) External conditions must not have too high an influence on the reaction: it is almost impossible to keep all the conditions exactly constant, especially when experimenting for a long time.
(8) Experimental varieties must be easily possible.
(9) The objects must be obtainable independent of place or season.
(10) Objects well studied biologically are preferable.
(11) Biological and experimental technics must not be too intricate.
(12) On radiotechnical considerations the object ought to be of small size.

In connection with these requirements, the eggs of *Drosophila*, as also the human skin, are well suited. As for the human skin, this object does not comply with the twelfth condition, so that scattering and absorption proportions of different qualities of radiations and sometimes even with different individuals, will possibly give difficulties.

Further, I investigated some chemical reactions, as, for instance, the alternation of the oxidation-reduction potential of quinone and methylene blue under the influence of radiation and the blackening of the photographic film. Eventually I studied the alteration of the oxidation-reduction potential of human serum by irradiation.

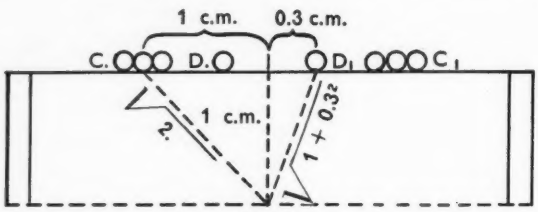


Fig. 3.

EXPERIMENTS WITH *Drosophila* EGGS

Technics.—There are numerous stems originating from the *Drosophila melanogaster* "wild." I chose "Black 12," and cultivated it by mass breeding. For this purpose a number of pairs were put in a cylindrical glass on the bottom of which was a layer of a food-mixture consisting of agar, banana, and yeast. Later, I preferred a mixture of agar, treacle, and refined cornmeal. The bottle was closed by a plug of cottonwool, without splits, since the flies always creep into them. By rotating the bottle obliquely, before the banana-agar coagulated, the wall of the bottle becomes covered by a thin layer of the food, on which the flies by preference lay their eggs.

These eggs, some tenths of a millimeter long, have a skin of chitine surrounded by dried follicle cells, which can still be recognized on their surface as small hexagons. They possess two tiny horns, and at one end a small canal, through which the spermatozoid can enter the egg. Under normal conditions the eggs hatch at room temperature in about 36 hours, some within 24 hours, others in two or three days. The born larvæ, at first very small, grow in the culture by eating yeast and by absorbing liquid. This growth, depending in rapidity on temperature and other circumstances, lasts about eight days, in which a length of from 0.5 to 1 cm. is reached. After that, each larva envelops itself in an armor of chitin. After ten days there appears out of this so-called pupa an adult fly, which is sexually mature within three or four days. The size of the fly is determined by the size of the pupa, depending upon the size of the larva, which is partly fixed by outward circumstances. The flies live about fifty days and can produce some hundreds of eggs. They thrive best at a constant temperature of about 21° C.

In order to collect eggs for my experiments, I proceeded as follows: Some pieces of paraffined paper, provided with little squares of 1 cm. drawn with a lead pencil, were moistened, stuck against the wall of a cylindrical bottle, and smeared over with the above feeding-mixture by means of a little brush. After the mixture had congealed and the superfluous food and moisture removed, one or more colonies of flies were put into the "lay-house" by shaking. I left the flies in the "lay-house" for from half an hour to two hours, according to the number of flies and the zeal with which they laid their eggs. Afterwards I shook them into a second "lay-house" or into their "dwelling-house," as the circumstances demanded.

It is possible to make the flies lay eggs for several days at a stretch, provided care be taken that there is always fresh, sweet-smelling food in the "lay-house."

In this connection I will describe some psychological peculiarities. Every ten days we used to give the flies a new "dwelling-house." Gradually, however, it turned out that, when the little insects just had a new place of abode, they were very little in-

clined to deposit their eggs in the "lay-house." We, therefore, left them a little longer in their houses, hoping to compel them in this way to lay all their eggs in the desired place. But in that case other factors must be taken into account. For instance, the number of eggs produced is dependent on the quality of the food, so that the flies of older cultures, the food of which becomes insufficient and unsavory, lay but few eggs. In addition to this, the flies then keep their eggs in the uterus for a long time; consequently, when they lay them, the larvæ are born immediately or within a few hours in a great percentage. Such a variety renders the eggs far from fit for our experiments, for which it is of the highest importance to have eggs of a definite age and in not too advanced a phase of development, individuals of different age being differently sensitive. Moreover, it is known that the flies lay their eggs best when it is dark.

After overcoming all difficulties and having collected on our slips of paper a sufficient number of eggs, varying from some tens to some hundreds, we can start our experiment. First of all, we counted the eggs, and it is for this very reason that we provided the slips with little squares; in this way it is possible to count the eggs with a very fair degree of accuracy.

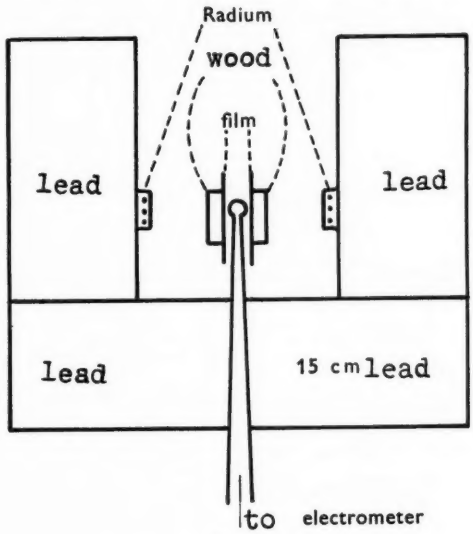


Fig. 4.

The slips were immediately laid in a Petri dish, and the dish was placed upon a black paper. The white eggs contrast clearly with the black paper; as a rule, I took a strong light, in order to be able to observe the eggs better. The counting was performed with the aid of a binocular microscope. Very often, especially at first, the counting was done by two persons. Thereupon the Petri dishes, on which were labels giving date and age of the eggs, kind of flies, and nature of the experiment, were covered. Moreover, wet wads of cotton-wool were laid inside for the purpose of preventing the agar and eggs from drying up. As soon as we started the experiment we could take such a paper and irradiate it.

For the irradiation we constructed a little wooden frame with a window of celluloid (washed film) which we moistened slightly lest the eggs should dry up during the irradiation. This window, fixed in a stand, could then be brought into any desired position.

After the irradiation the slips of paper were laid again in the Petri dish and kept

at room temperature. Then we counted the number of larvæ hatched after about 24, 48, and 72 hours, and later on occasion-

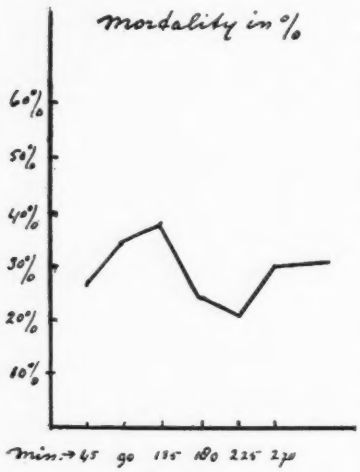


Fig. 5.

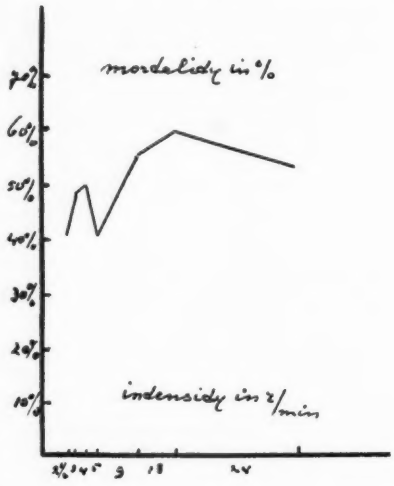


Fig. 6.

ally after 96 hours, by means of a binocular microscope, and these were removed with a fine pair of tweezers. The number of non-hatched eggs, after correction for spontaneous mortality, showed the rate of mortality due to irradiation. The *Drosophila* eggs are highly radiosensitive, and the spontaneous mortality is very slight—Packard stated 3 per cent on an average; we found about 12.5 per cent. This mortality depends on the dose; for instance, when using increasing doses, all the eggs do not die at the same point; there is even a gradual transition, which we can represent by a S-shaped curve.

It turns out that there is a small threshold dose, whereas a mortality of 100 per cent can be obtained only when taking a very high dose. In the many experiments I made there were always numerous deviating results, in evident contrast to those of some other research workers, who found very constant rates of mortality for any one dose. Some recently published researches have confirmed my statement. It is obvious that it is not possible to place a high value on one experiment. In my opinion, the biological variety of the eggs accounts for these varying results. However, by making a great many experiments, an average could be calculated which always suited the curve.

Ascertaining the figures of mortality, we counted the eggs hatched daily, mostly on three, sometimes on four, successive days. The eggs hatched within 24 hours—sometimes a few minutes or hours after they are laid—have, in our opinion and in that of other writers, been kept too long in the uterus, and are therefore too old for the experiments. They are no longer highly sensitive in these advanced phases of development. Consequently, for our final results we shall have to take this factor into account, and accordingly subtract these eggs from the total number, before calculating our percentage of mortality. The eggs hatched on the second and third days are the eggs not seriously damaged. The proportion of the number of eggs hatched on the second day to the number of the third day, is, however, partly determined by outward circumstances (for instance, differences in temperature), and so it will be essential not to neglect the hatching of the eggs on the third day, unless the eggs are kept in a thermostat exactly at

constant temperature (18° C.). The correction for the eggs which are too old and less sensitive may take place only if the eggs are kept at not too high a temperature, as otherwise many eggs which are not too old would hatch within 24 hours. On the fourth day we removed all agar from the slips of paper in order to discover the larvæ hidden deep in the agar, in this way checking the former counts.

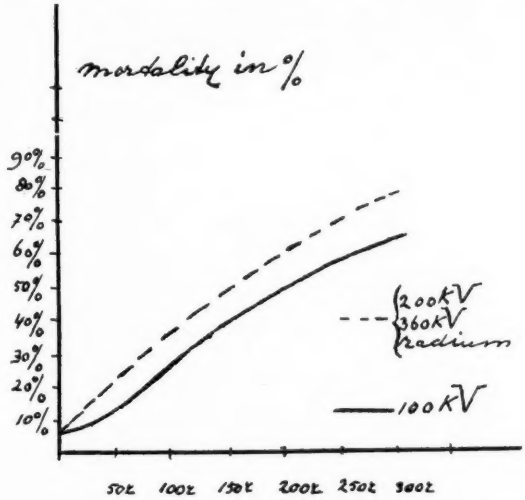


Fig. 7.

TABLE IV.—EXAMPLE OF THE INFLUENCE OF TEMPERATURE ON RAPIDITY OF HATCHING

	Kept at 23° C.	Kept at 16° C.
Total number	42	35
Hatched after 1 day	24	8
	18	27
2 days	13	18
	5	9
3 days	2	4
	3	5

At the same time, in studying the material it appeared that the eggs first laid on a certain day had better not be used for experiments, since these eggs are often somewhat older on an average than those of the next lay, which may cause some irregularity in the results. In my experiments this proved to be insignificant, but it is wiser to avoid it. At any rate, such irregularities are remarkably diminished by the correction of the eggs hatched within the first 24 hours.

Often it is not possible to perform the experiments at the same time, so that the portions irradiated with different qualities had to wait more or less long, and therefore showed different stages of development, especially as the early stages of the development show a startling rapidity. The question arose as to whether errors might yet have slipped in, owing to this difference in age. To answer this question we irradiated with the different qualities in reversed order, without finding any noticeable difference in the results.

TABLE V

	Dose	Low K.V. irr. first mortality in %	High K.V. irr. first mortality in %
High K.V. (200 K.V., 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al)	50 r	27½	36
	100 r	37	56
	150 r	58	76
	200 r	76½	83
	300 r	76	89
Low K.V. (100 K.V., 0.5 mm. Cu)	50 r	27½	20
	100 r	28	42
	150 r	48	64
	200 r	63½	76½

The results in this table neutralize each other; from the upper half the conclusion

would be justified that the eggs first irradiated are the more sensitive, while from the lower half of the table the reverse conclusion might be drawn. This is, of course, connected with the question as to whether or not it matters how long the eggs were laid before their irradiation. It may happen that, owing to practical difficulties, the eggs cannot be irradiated immediately. Therefore, I made a series of experiments whereby separate portions of eggs were irradiated at regular intervals.

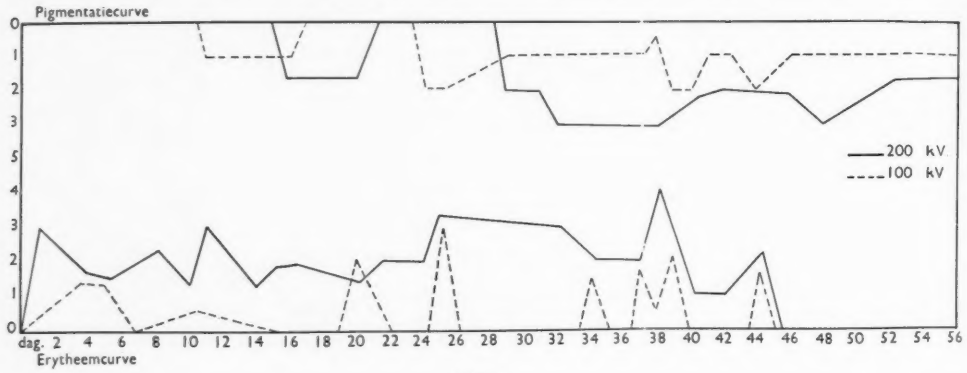


Fig. 8.

TABLE VI.—MORTALITY BY 100 r AT 180 K.V., 0.5 MM. CU

Time after Taking Eggs Out of Lay-house	No. Eggs Not Hatched: Total No.	Mortality in %
15 min.	497/1603	27½
30 min.	262/864	30
45 min.	438/1609	27½
60 min.	301/1115	27
75 min.	560/1574	35½
90 min.	484/1407	34½
105 min.	775/1856	41½
120 min.	256/759	35½
135 min.	626/1693	37
150 min.	387/1021	37½
165 min.	518/1746	30
180 min.	204/810	25
195 min.	516/1854	28
210 min.	218/805	27
225 min.	406/2063	20½
240 min.	192/755	25
255 min.	373/1359	27
270 min.	345/1155	30
285 min.	421/1376	30½

In Table VI and in Figure 5, the results are shown from which we see, as stated by Packard, that the eggs are the most sensitive about two hours after they are laid. Since I nearly always carried out my experiments between forty-five minutes and two hours after the lay, I am of the opinion that I did not make any great errors. Still, one may profit by these experiments to limit deviations.

Another question arising is, whether difference of intensity can influence the effects. It is known, and especially emphasized in modern literature, that a definite dose given within a short space of time, *i.e.*, with a high intensity, produces a stronger effect than one with low intensity. However, the limits beyond which this phenomenon appears are not quite determined, and, in my opinion, will differ with various objects.

To solve this question in the matter of *Drosophila* eggs, I also made experiments, the results of which are recorded in Table VII and Figure 6.

The numbers are not wholly convincing, but with the exception of a single figure, which may always be expected in biological tests made during a long period, we can state that under three to four r per minute the same dose becomes less active. In view of this experience, I worked as much as possible with radiations of equal intensity.

The chief part of the research was executed in such a way that I obtained a mortality curve for each type of radiation by exposing portions of eggs separately to different doses. As a rule we used doses of 50 r, 100 r, 150 r, 200 r, 300 r.

Table VIII states the total number of

eggs irradiated with the suitable dosage. No correction has been made for the wave length dependency of the dosimeter at 360 K.V. and radium, but it is made for the deduction necessary for the old eggs.

Now, making the correction for the wave length dependency at 360 K.V. and γ-rays of radium, we arrive at the following figures (Table IX and Figure 7).

The figures for the higher tensions and for radium fall along one line, which is on a somewhat higher level than the curve for 100 K.V. These experiments leave the impression that shorter wave lengths have a somewhat greater effect than long wave lengths.

EXPERIMENTS ON ERYTHEMA OF THE HUMAN SKIN

The human skin has an undulating reaction, often with several tops. In this reaction, too, the time-factor plays a rôle, so that it is advisable to irradiate with equal intensities. Owing to technical and practical difficulties, I did not make any observations with radiation of 360 K.V., only comparing the other investigated three types of radiation regarding the erythema dose. I distinguished five degrees of reaction: degree (1) vague; (2) light pink; (3) pink; (4) red; (5) dark red.

In these experiments the pigmentation

TABLE VII

Time for 150 r	1½′	2½′	5.75′	11.46′	16′	31′	39′	45′	59′
Intensity	100 r/min.	60 r/min.	24 r/min.	13 r/min.	9 r/min.	5 r/min.	4 r/min.	3 r/min.	2.5 r/min.
Mortality on total	852/1805	1154/2022	837/1679	791/1351	1041/1872	761/1960	1101/2200	885/1862	1496/3642
Percentage	47	56	50	58	55	39	50	47.5	41

TABLE VIII

	50 r Total Mort. %	100 r Total Mort. %	150 r Total Mort. %	200 r Total Mort. %	300 r Total Mort. %
100 K.V., 0.5 Cu	3020–807–**27**	2791–867–**31**	4551–2427–**53½**	3319–2270–**68**	3077–2539–**82**
200 K.V., 1.5 Ag + 0.2 Cu + 0.5 Al	3367–972–**29**	3111–1286–**41**	4908–3197–**65**	7505–6051–**80½**	7588–5984–**79**
					250 r
360 KV., 2 Sn + 1 Cu + 1 Al	890–264–**30**	3332–1158–**35**	3500–1821–**52**	3831–2520–**66**	3520–2435–**69**

Radium

180 r Total Mort. %	360 r Total Mort. %	540 r Total Mort. %	900 r Total Mort. %
2168–1216–**56**	2736–2209–**81**	2163–1834–**84**	1243–1184–**95**

TABLE IX

Dose int.	100 K.V.	200 K.V.	360 K.V.	Radium
40			890–264–**30**	
50	3020–807–**27**	3367–972–**29**		
80			3332–1158–**35**	
100	2791–867–**31**	3111–1286–**41**		
120			3500–1821–**52**	
135				2168–1216–**56**
150	4551–2427–**53½**	4908–3197–**65**		
160			3831–2520–**66**	
200	3319–2270–**68**	7505–6051–**80½**	3520–2435–**69**	
270				2736–2209–**81**
300	3077–2539–**82**	7588–5984–**79**		
405				2163–1834–**84**
675				1243–1184–**95**

which appeared somewhat later was duly marked; three degrees were noted: (1) vague; (2) light brown; (3) dark brown.

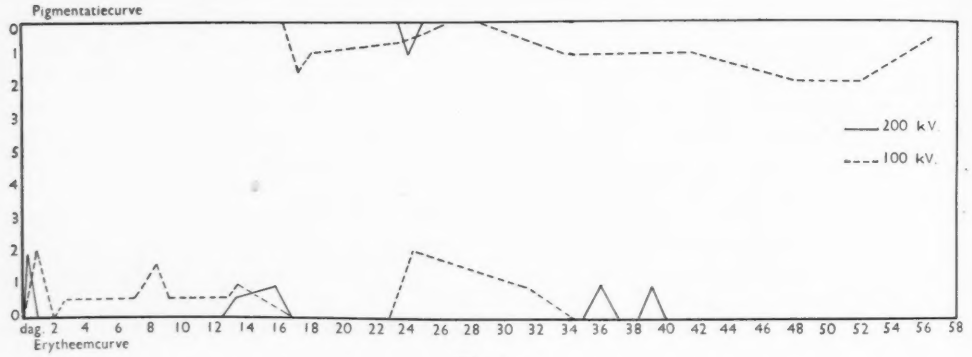


Fig. 9.

From preliminary tests it appeared to me that I could show a difference in dosage of 12.5 per cent, while I ascertained at the same time that within not too long exposure times a difference of intensity of one to two had no distinct influence on the reaction, so that I could experiment within wider limits. I exposed the skin of one patient to at least two types of radiation practically simultaneously. When experimenting, I paid special attention to the erythema curves, which are the easiest to analyze, and chiefly founded my conclusions on them. The curves below represent the results.

Case 1. Man, 55 years of age; good general condition. On the fore side of the left thigh a field 8 × 8 cm. was irradiated with 500 r (100 K.V.; filter, 0.5 mm. Cu). On the fore side of the right thigh a field 8 × 8 cm. was irradiated with 500 r (200 K.V.; filter, 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al). During irradiation the dose was controlled continuously. Irradiation of the two fields was done in one performance.

Observing this patient (Fig. 8), a noticeably stronger and more lasting reaction was to be seen after irradiation at 200 K.V. Here the tops of the curve of 200 K.V. are much higher (Fig. 8). If one had to estimate the difference in dose from the grade of the erythema and pigmentation, one could fix the difference at 20 per cent. The erythema waves last, in all, for about six weeks. In strong reactions the pigmentation remains for months.

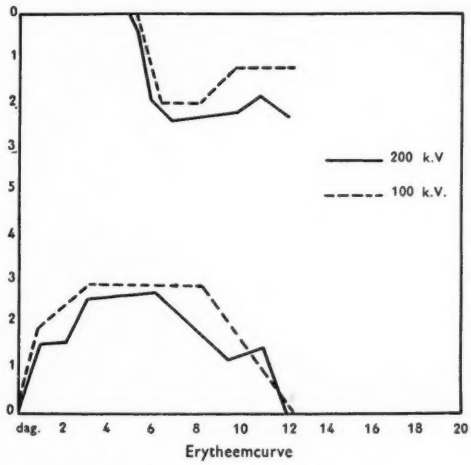
Case 2. Woman, about 60 years of age; moderate general condition. On the right groin a field 8 × 8 cm. was irradiated with 500 r (100 K.V.; filter, 0.5 mm. Cu). On the left groin a field 8 × 8 cm. was irradiated with 500 r (200 K.V.; filter 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al). During irradiation the dose was controlled continuously. Irradiation of the two fields was done in one performance.

Observing this patient (Fig. 9), who received the same dose as Case 1, we note a very much slighter reaction following both irradiations, with a somewhat stronger erythema and a slightly darker pigmentation at 100 K.V., 0.5 mm. Cu filtration.

Case 3. Man, 40 years of age; rather bad general condition. On the fore side of the right thigh a field 8 × 8 cm. was irradiated with 600 r (100 K.V.; filter, 0.5 mm. Cu + 3 mm. Al). On the fore side of the left thigh a field 8 × 8 cm. was irradiated with 600 r (200 K.V.; filter, 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al).

This patient (Fig. 10) was irradiated with a somewhat higher dose, as the reactions of the skin of the last patient were on the whole so slight that the determination of the grade of intensity was difficult. Though the reaction has not been observed for a

long time, as the patient left the hospital, it is still quite possible to compare the intensity of the reaction, as the rather high primary reaction (*frühreaktion*) is stronger at 100 K.V. The main reaction is, on the contrary, somewhat more intense at 200



Erytheemcurve

Fig. 10.

dose had caused a very distinct erythema and pigmentation. Here, too, one notices a small difference in favor of the long waves.

Case 4. Man, 30 years of age; bad general condition. The fore side of the right thigh was irradiated with 600 r (100 K.V.; filter, 0.5 mm. Cu). The fore side of the left thigh was irradiated with 600 r (200 K.V.; filter, 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al). Here the reactions were nearly equal, but slightly stronger at the higher kilovoltage (Fig. 11).

Case 5. Man, 70 years of age; rather good general condition. The right groin region was irradiated with 600 r (100 K.V.; filter, 0.5 mm. Cu). The left groin region was irradiated with 600 r (200 K.V.; filter, 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al). This patient (Fig. 12) showed a nearly equal reaction for both qualities, but somewhat stronger at 100 K.V.

Case 6 (Fig. 13). Woman, 60 years of age, in rather bad general condition. The fore side of the right thigh was irradiated with 600 r (100 K.V.; filter, 0.5 mm. Cu). The fore side of the left thigh was irradiated with 600 r (200 K.V.; filter, 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al). The so-called K.V., so that we might conclude a practically equal reaction of a slightly different type.

Case 7 (Fig. 14). Woman, 50 years of age, in rather bad general condition. The fore side of the right thigh was irradiated with 600 r (100 K.V.; filter, 0.5 mm. Cu). The fore side of the left thigh was irradiated with 600 r (200 K.V.; filter, 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al). The primary reaction, though very slight, is the same at the two types of rays. The secondary erythema reaction is somewhat stronger at 100 K.V., but the pigmentation is more marked at the higher kilovoltage. Still, one can conclude that both reactions are practically equal.

Case 8 (Fig. 15). Man, 45 years of age, in rather bad general condition. The fore side of the left thigh was irradiated for 165 minutes with 140 mgr. of radium on a table-shaped applicator. Not far from this area a field 8 × 8 cm. was irradiated with 600 r (100 K.V.; filter, 0.5 mm. Cu, for 100 minutes). The first wave of the radium reaction is much stronger than the wave of the roentgen reaction. The second wave does not show an important difference. (It

was impossible to continue the observation, as the patient left the hospital.) This reaction agreed with more than 600 r; that conclude that the radium applicator gives more than 3.6 r per minute.

These erythema tests suggest that the

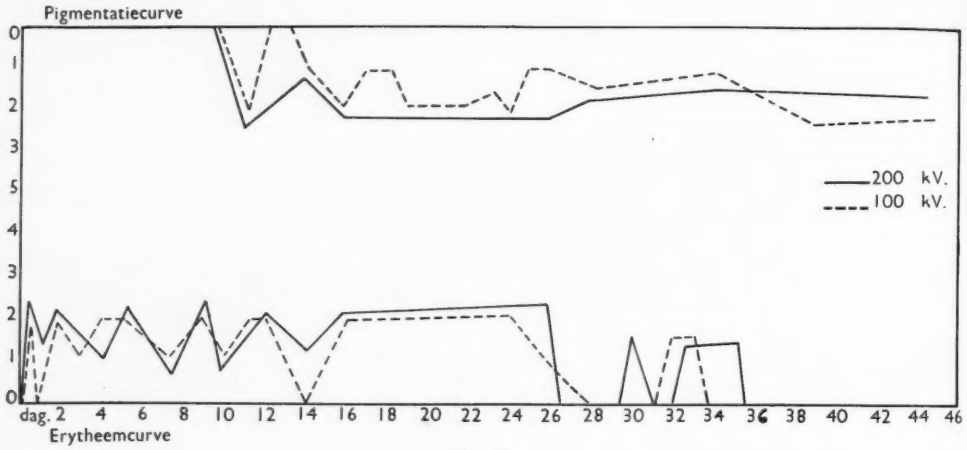


Fig. 11.

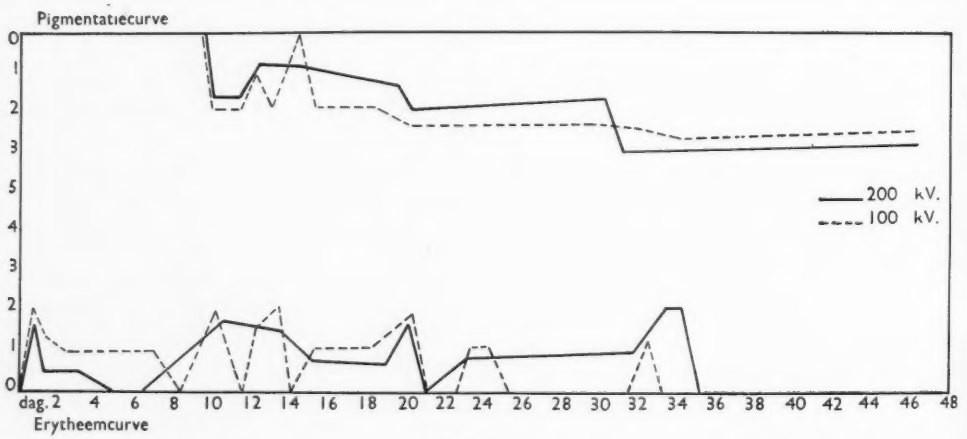


Fig. 12.

means that the intensity of our radium applicator was more than 3.6 r per minute.

Case 9 (Fig. 16). Woman, 60 years of age, in rather bad general condition. This case was irradiated under the same conditions as the last patient.

Here, too, one can see a distinctly stronger radium reaction in the first wave as well as in the second wave. The pigmentation caused by the radium applicator is stronger, too. Remarkable are the many little erythema waves. Here, also, one can biological effect is proportionate to the ionization power of the rays. The radium erythema seems to be less intensive than the roentgen reactions, but then we must not forget that this radium applicator (the small table with 140 milligrams) homogeneously irradiates only a very small surface, as also that the depth dose is very slight. The effect on the deeper tissues and vessels will no doubt be of some moment for the appearance of an erythema, so that it is rather remarkable that, in spite of the small

depth dose, the erythema produced by our applicator corresponds so well to the dose, as calculated by us.

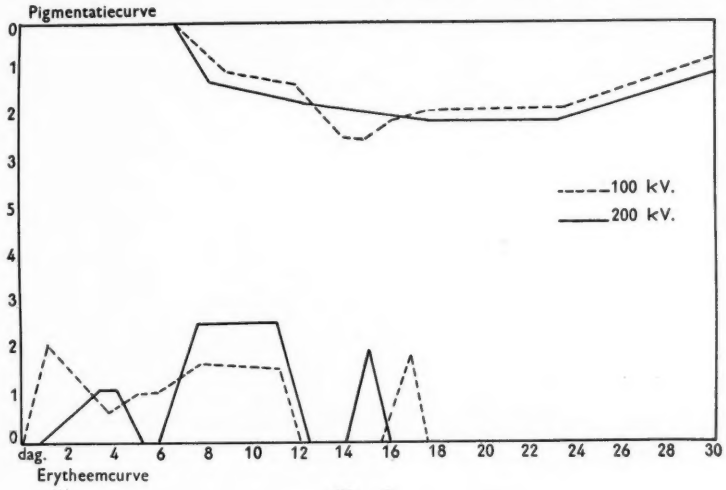


Fig. 13.

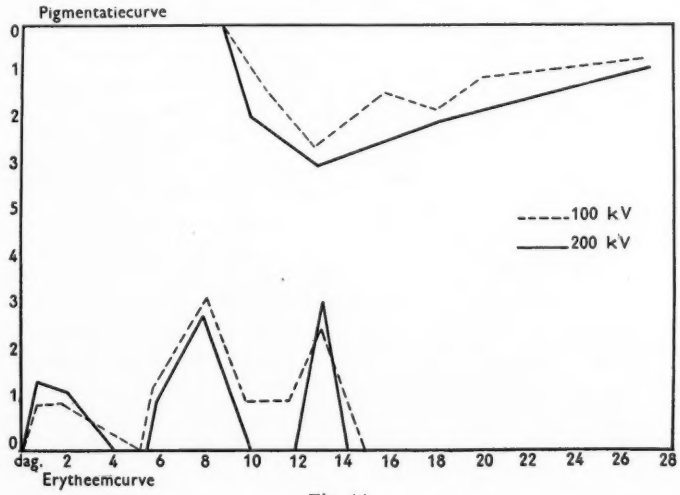


Fig. 14.

CHEMICAL EXPERIMENTS

In making these chemical experiments I had, from various technical and practical considerations, to restrict myself to the investigation of two types of radiation, namely, 100 and 200 K.V. Assisted by Dr. Waterman, who has largely experimented on this subject, I examined the change in the oxidation reduction potential by irradiation of certain solutions of chemicals. By the oxidation reduction potential of a certain solution we understand the tension which is measured by dipping an electrode of a precious metal (for example, platinum or gold) into this fluid, taking care that the hydrogen ion concentration (P_H) is kept constant. This potential is usually measured in comparison with a hydrogen electrode or a half-element of well-known potential, as the calomel electrode. That this potential is connected with reduction and oxidation processes will be clear when we

consider that, in modern chemistry, we understand by oxidation and reduction loss or increase of negative charge (electrons) of

We followed the technical method of these workers. A narrow funnel-shaped glass vessel is closed at the bottom by an

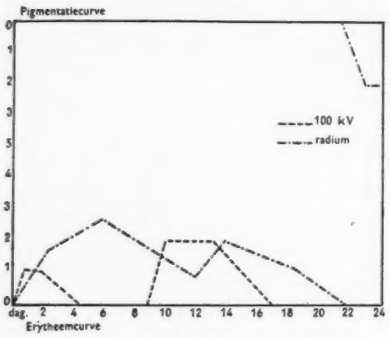


Fig. 15.

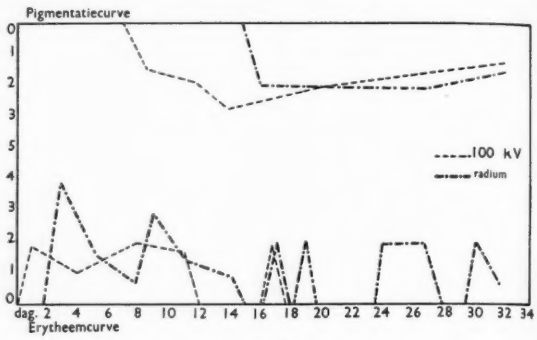


Fig. 16.

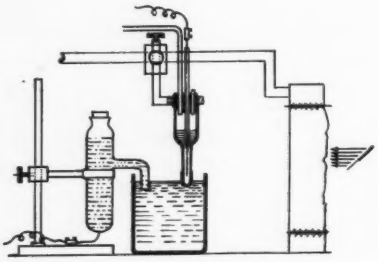


Fig. 17.

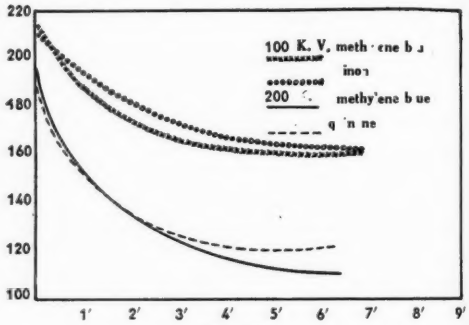


Fig. 19.

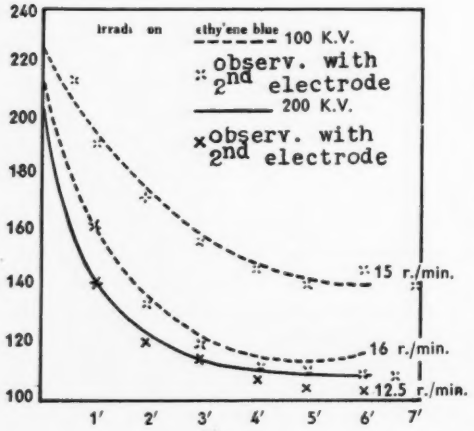


Fig. 18.

an atom. So oxidation must result in a rise, reduction in a fall, of potential. This tension, called redox-potential, can be strongly influenced by irradiation (Waterman and Limburg).

agar KCl stopper. The fluid to be tested is poured into the tube, and the electrode is fixed in it through a rubber stopper perforated in three places (Fig. 17). Two of these openings serve for letting pure nitrogen pass, so that the oxygen of the air cannot have any share in the reaction.

The electrode is connected by a long conducting-wire with a potentiometer placed outside the roentgen room; the bottom side of the tube dips in a Petri dish with 3 N KCl. The same Petri dish communicates with the calomel electrode, which is in connection with the potentiometer, so that *via* this meter the chain is closed and the redox-potential can be read on this instrument. Next I tested: (1) methylene blue, which was converted into leuko-methylene blue; (2) quinone, which can be reduced into hydro-quinone. Ex-

amples of the action of both types of radiation are illustrated by the curves below (Fig. 18).

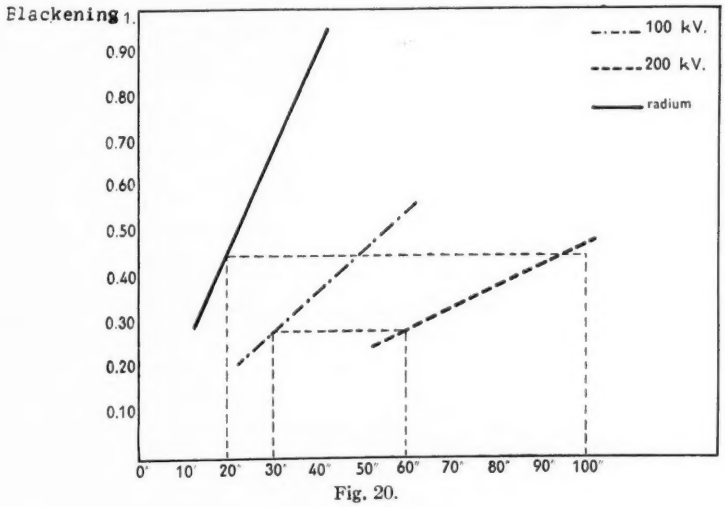


Fig. 20.

For Curve 18 I used a solution of methylene blue 1/20,000, 100 K.V. roentgen rays and 200 K.V. roentgen rays.

For the curves of Figure 19 I used a solution of methylene blue of 1/20,000 and phosphate buffer of P_H 6.8 and a quinone solution of 1/50,000 in phosphate buffer of P_H 6.6. The intensity of the irradiation of 100 K.V. was 17 r a minute, of 200 K.V., 18 r a minute.

From this test, supported by other similar experiments, I came to the conclusion that in this physico-chemical reaction we have to see a difference in favor of hard rays, as revealed by a more rapid fall of the potential (more sloping curves) and in a greater fall, whereby the equilibrium attained is lower.

Summarizing the above results, we find in this physico-chemical reaction a difference in effect of about 25 per cent in favor of hard rays.

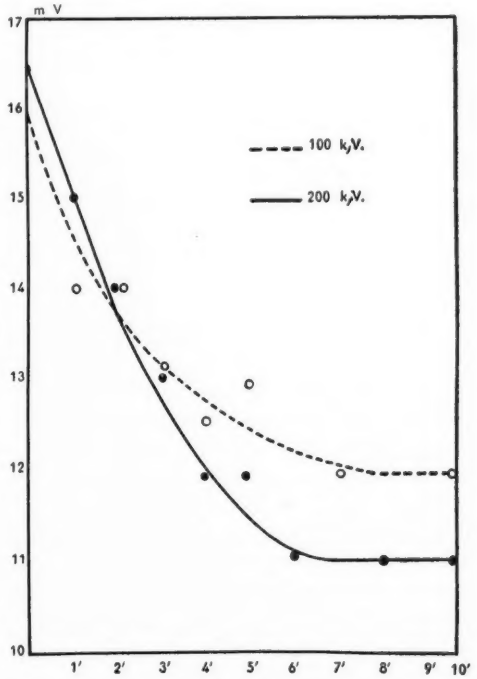


Fig. 21.

PHOTOGRAPHIC MEASUREMENTS

The blackening of a photographic plate is defined as follows: I_0 being the intensity of a bundle of light which falls on a plate and I that of the light transmitted, the blackening $Z = \log \frac{I_0}{I}$. In this connection we speak of "Blackening 1," if the blackened plate transmits only a tenth of the light, while "Blackening 2" indicates

that no more than 1 per cent is transmitted. Z is a function of the intensity of the incident rays and the time of exposure; thus, in general, $Z = f(I.t.)$. According to Schwarzschild, $Z = f(I\,t^p)$ in case of visible light, in which p is smaller than 1. As regards roentgen rays, Bouwers has proved that p is almost equal to 1; the same statement was proved by Stoel and myself as to γ-rays. Here the formula of Bunsen-Roscoe, $It = C$, holds good. These formulas, of course, can be applied only to rays of equal quality; with respect to rays of diverse wave lengths, absorption plays a great rôle, so that an equal number of r of different quality will no doubt produce a different blackening.

Bouwers and van der Tuuk note certain numbers (Table X) for a special kind of film under definite conditions of development.

TABLE X.—NUMBER OF r REQUIRED FOR $z = 0.5$

Tension in K.V.	Filter		
	1 mm. Pb + 1 mm. Cu + 1 mm. Al	1 mm. Cu + 1 mm. Al	1 mm. Al
190	**0.120**	0.052	0.026
180	0.100	0.048	0.024
160	0.080	0.040	0.020
140	0.065	0.030	0.018
120	0.050	0.026	0.018
100	0.040	0.021	0.017
80	0.030	**0.018**	0.016

These differences found experimentally may be explained by the fact that by increasing penetrating power the absorption in the film decreases relatively far more than in the air of the ionization chamber. Such is self-evident, considering that in this spectral range the real absorption in the film still plays a great rôle. This true absorption is dependent on λ^3, whereas in the air the absorption is caused by scattering, the latter being practically independent of wave length. In absolute sense, the numbers are dependent on the kind of film (sensitivity), and on the developmental conditions.

And what about these relations in regard to our types of radiation? To answer this question I compared the blackenings obtained with 100 K.V. and 200 K.V.

TABLE XI

Used: Doneofilm; standard developer. Blackenings were measured with a stufometer

Type of Radiation	Exposure Time in Seconds	Blackening after Subtraction of Control
100 K.V., 0.5 Cu, 3 ma., focal distance, 2 meters	30	0.27
	40	0.33
	50	0.44
200 K.V., 1.5 Ag + 0.2 Cu + 0.5 Al, 3 ma., focal distance, 1 meter	60	0.29
	80	0.39
	100	0.46

Converting the numbers in Table XI into curves, we see that the blackening obtained in 60 seconds at 200 K.V. is equal to that of 30 seconds at 100 K.V. It appeared from ionization measurements that 30 seconds at 100 K.V. correspond to 0.08 r, whereas in 60 seconds at 200 K.V. we got 0.48 r; in other words, = six times as many r are wanted for the same blackening. (See Table X: the numbers marked correspond to our type of radiation.)

Since the radiation emitted at 100 K.V., 0.5 Cu has an average wave length of about 0.2 Å., and radiation produced at 200 K.V. has an average wave length of 0.08 Å., it would be expected, if we had to do only with the absorption that the number of r for blackening at 200 K.V. would be $\left(\frac{0.2}{0.08}\right)^3 = 15$ times as high as at 100 K.V. That we did not find such a high factor can be ascribed to the fact that, in using these very hard rays, the scattering, especially in the gelatine and the celluloid of the film, is noticeable.

For the photographic experiments with radium, I used our table-shaped applicator. On the strength of our measurement described before, we assumed that the intensity of the γ-rays from this source amounted to about 5 r per minute.

Exposure of 20 seconds produced a blackening of..... 0.43

Exposure of 40 seconds produced a blackening of..... 0.95

Thus, in 20 seconds exposure with our radium applicator we get the same blackening as in 100 seconds exposure at 200 K.V., the latter corresponding to 0.8 r. Our radium applicator emits in 20 seconds a dose of 1.7 r, so that the γ-rays appear to have half the blackening capacity at a similar number of r. That in spite of the great difference in wave length this proportion is not greater, can be explained by the phenomenon that scattering prevails in cases of very short wave lengths and real absorption sinks into the background.

Summary.—The blackening of photographic films by roentgen and radium rays is not proportional to the dose of rays measured by ionization. The harder the rays, the smaller the blackening capacity.

SEROLOGICAL EXPERIMENTS

Many research workers have been engaged on the changes in blood serum after irradiation. In general, serum *in vitro* was irradiated, but others investigated the blood of irradiated humans or animals. All kinds of determinations were made, as, for instance, observations on the albumen composition, cholesterine content, fermentative and bactericidal qualities, and acid-base equilibrium: in short, nearly all possibilities were looked into. It is a pity that the observations of many research workers contradict one another, and it frequently occurs that but scant attention is paid to dosimetric and qualitative differences of the rays.

In connection with the work of Dr. Waterman, and with his assistance, I performed observations of the redox-potential of human serum. Dr. Waterman demonstrated that carcinomatous serum has a high redox-potential, and can be strongly influenced by irradiation, in contrast with serum of sufferers from other chronic diseases, and of normal persons, whose sera are very constant. Accordingly, carcinomatous serum was irradiated with 100 K.V. and 200 K.V., at an equal intensity of 16 r per minute. One of our observations—all furnishing similar results—is elucidated in the curve shown in Figure 21.

Judging from these observations, I was able to state a somewhat stronger effect of the harder rays, represented by a greater and more rapid declination of the curve.

SUMMARY

A comparative investigation was carried out with:

1. Roentgen rays emitted at 100 K.V., filter of 0.5 mm. Cu.
2. Roentgen rays emitted at 200 K.V., filter of 1.5 mm. Ag + 0.2 mm. Cu + 0.5 mm. Al.
3. Roentgen rays emitted at 360 K.V., filter of 3 mm. chrome iron + 2 mm. Sn + 1 mm. Cu + 2 mm. Al.
4. Gamma rays from radium, filter of 0.5 mm. Fe + 1 mm. Pb.

Theoretical and experimental dosimetric comparisons were made with the following phenomena as indicators:

1. Mortality of *Drosophila* eggs.
2. Erythema of the human skin.
3. Blackening of the photographic film.

TABLE XII

Object	Material	Effect	100 K.V.	200 K.V.	360 K.V.	Radium
Siemens Dosimeter carbon-walled chamber	physical	ionization	1	1.125	1.20(?)[2]	1.35 (?)
Drosophila eggs	biological	death	1	1.24	1.24(?)	1(?)
Human skin	biological	erythema	1	±1	....	±1(?)
Oxidation reduction potential (quinone, methylene blue)	chemical	lowering of potential	1	1.3	....	....
Photographic film	chemical	blackening	1	0.16[1]	....	0.08[1] (?)
Oxidation reduction potential of serum	seriological	lowering of potential	1	>1	....	....

[1] These results refer to equal incident energy.
[2] The mark of interrogation indicates that the results were partly obtained by reasoning and have not been completely established by experiment.

4. Oxidation reduction potential of methylene blue and quinone.
5. Oxidation reduction potential of carcinomatous serum.

Table XII shows the results of this investigation in relative degrees of effect in respect to the action of the radiation at 100 K.V. filtered through 0.6 mm. Cu.

Conclusion.—These tests plead for the theory that in radiation with roentgen rays with a wave length shorter than 0.1 Å., or with gamma rays, no selective chemical, biological, or seriological reactions in a qualitative sense occur. In a quantitative sense, the conclusion may be drawn for the present that there is a somewhat stronger action of the harder rays for the same quantity of absorbed energy.

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MULTIPLE ENDOTHELIOMAS OF THE SKIN WITH METASTASIS

REPORT OF CASE

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THE subject of endothelioma, a term first advanced by Golgi, in 1869, in describing a calcified neoplasm of the dura mater, an endothelial psammoma, forms one of the most notable topics in pathology. No chapter is more incomplete. With our meager conception of the reticulo-endothelial system, and the group of composite tissues which it composes, it is not surprising that this field should offer fertile soil for forensic deliberation among pathologists. Research, directed toward studying the histogenetic origins and capacities for variable differentiation characterizing the least understood of cell groups, would accomplish much toward settling the questions at issue.

Endothelioma of the meninges, pleura, and peritoneum is characteristic, and has been accepted as authentic. Marckwald's (1) case of multiple endotheliomas of the bones is recognized by Ewing. Solitary diffuse endothelioma of the bone, or Ewing's sarcoma, is a definite entity. Multiple and single endotheliomas of the lymph nodes have been described and reported. Recklinghausen in 1897, first recognized primary endothelioma of the lymph nodes as a distinct tumor. Ewing (10) became enthusiastic in the study of these tumors, reported a number of cases, and published a monograph on the subject in 1913. However, his recent studies would show that it is still a medical curiosity. Only a few cases have been recorded in the last two decades. Its incidence varies in different medical centers, which factor is governed by the diversity of opinion as regards the true nature of endothelioma, and the hesitation of some pathologists to make this diagnosis. If the neoplastic nodes are cervical in distribution, and the type of growth is alveolar, primary carcinoma of the nasopharynx, base of the tongue, that of branchiogenic origin, as well as bronchogenic carcinoma of the superior pulmonary sulcus, must be eliminated before concluding that the lesion is one of primary endothelioma and not metastatic cryptogenic carcinoma. McNamara (22) has recently reported five cases of the multiple type. In this article, McCartney's (14) and Zaffagnini's (15) cases with positive Wassermann are mentioned. This association of syphilis with endothelioma would recall Ewing's (10) contention that the disease is often excited by chronic granulomatous infections. While endotheliomas of the uterus, ovary, and stomach have been described, they have not been accepted as typifying the classical structure of this mesenchymal tumor.

No phase of the subject has suffered as much controversial discussion as that of endothelioma of the skin. Billroth first reported multiple primary malignancies seventy-five years ago, and they have long since ceased to be regarded as pathologic curiosities. Yet, primary endotheliomas of the skin, which are usually multiple, are rare, and do not appear in any of the tables compiled by Warren and Gates (21), in their recent survey and statistical study of the literature bearing on multiple primary malignancies. Substantial proof of their existence is denied by many pathologists, and most of the cases have lost their claim for recognition. They have been classified by critical observers as cylindroma and cellular nevi, derived from constricted anlage of embryonic epithelium situated in the skin. Others, such as the lymphangioma tuberosum multiplex of Kaposi, have been shown to arise from dilated sweat glands. Braun's celebrated case of cylindromatous structure was proven by Krompecher (6) to be of glandular epithelial origin, and designated as epithelioma adenoides cysticum. This

author refers to endothelioma of the skin as "carcinoma endotheliale." Fick (9) is very positive that genuine endothelioma cutis is a non-entity.

Many problems bearing on the etiology, pathology, and clinical symptoms of endothelioma of the skin remain unclear. This confusion may be partly explained by the rarity of the lesion, the unfamiliarity of most physicians with it, as well as a lack of appreciation of the fact that endothelial cells are capable of metamorphosis under changing environment. Under the influence of inflammatory processes, by increasing in number they may lose their typical form, and assume various bizarre shapes, with a corresponding alteration in the arrangement of the cell groups. With their dual nature, they may simulate either epithelial or connective tissue types, that is, they may resemble organoid or histoid growths. Embryologically, they are of mesenchymal origin, arise from the vascular endothelium or its constituents, and hold a position mid-way between the above two. Functionally, they have the ability to secrete mucin, hyaline, and amyloid material, thus imitating epithelium. On the other hand, they are capable of producing connective tissue structure in inflammations of the serous cavities, blood, and lymph vessels, as well as granulation tissue, with the formation of epithelioid and giant cells.

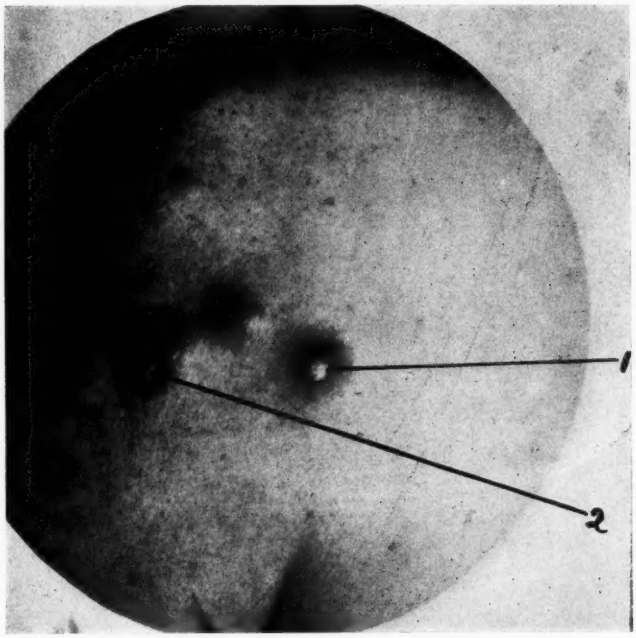

Fig. 1. Photograph of posterior aspect of left shoulder, showing the various types of skin lesions. The numerals, 1 and 2, indicate those nodules which ulcerated, and which were incised. These larger, raised growths varied in color from pink to a strawberry hue. Note the three smaller excrescences at the tip of the shoulder, lying deep in the dermis. They are representative of the lesions as they first appeared in the skin.

In 1906, Zeit (3) published an exhaustive and instructive article on the subject, which has received due praise by Hazen in his book on Skin Cancer. Zeit expresses the opinion that true endothelioma of the skin arises from the endothelium of the perivascular lymph spaces. His conception of the differential diagnosis between this lesion and carcinoma may be quoted as follows:

1. The endothelial cells are intimately connected with the stroma, and cannot be brushed out as in carcinoma. After fixation with its attendant shrinkage of tissue, the cells cling to the walls of the lymphatics.

2. The cells produce intercellular fibrils and cement substance, and form compact layers about the blood spaces.

3. Endothelial cell masses form a dense mosaic of many layers of cells, with small, sharply outlined nuclei, surrounded by a broad envelope of clear, glassy, perinuclear cytoplasm. The cytoplasm in epithelioma is granular and scanty, and the nuclei are relatively large.

4. Delicate fibrillar processes extend from the walls of the alveoli into the proliferating endothelial masses.

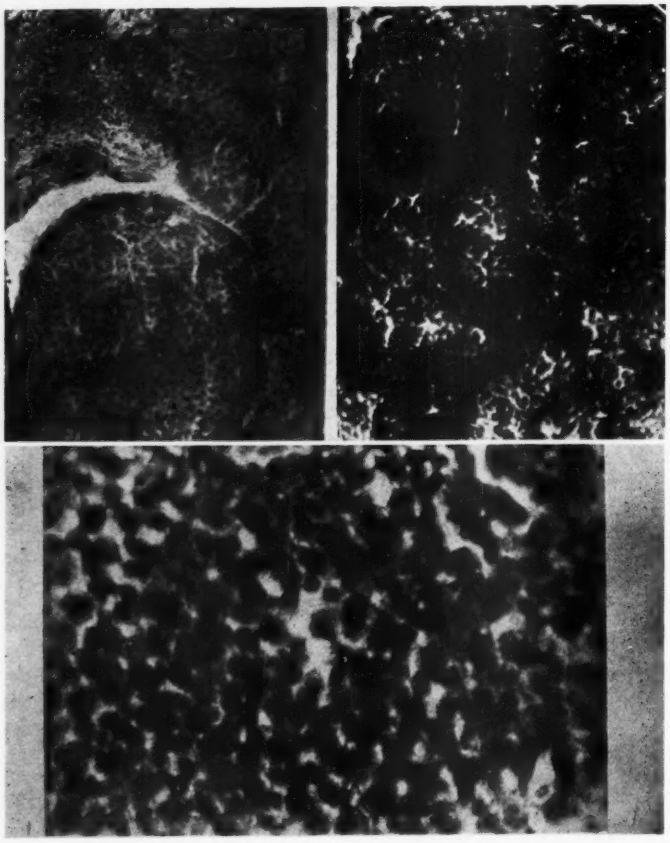

Fig. 2. Photomicrographs of original biopsy, showing a reddish mulberry-like lesion of the skin of right breast. *Above*, low power views showing the alveolar, compact arrangement of the cells. *Below*, high power view portraying the type of cell found. Note the mitotic figures, the glassy cytoplasm of some of the cells, the intercellular processes or fibrils, and the tapering of some of the cells into these processes.

5. The endothelial cells may be arranged in cords and cylinders, and separate out hyaline material, which picture characterizes cylindroma; or, they may form lumina-like or sieve-like areas, due to the secretory activity of the endothelium which may confuse the condition with myxoma.

6. Endothelioma may be distinguished

from sarcoma by its organoid structure as compared with the histoid structure of the latter.

of the trunk and extremities, may be involved. There is a definite tendency to decomposition, ulceration, and hemorrhage,

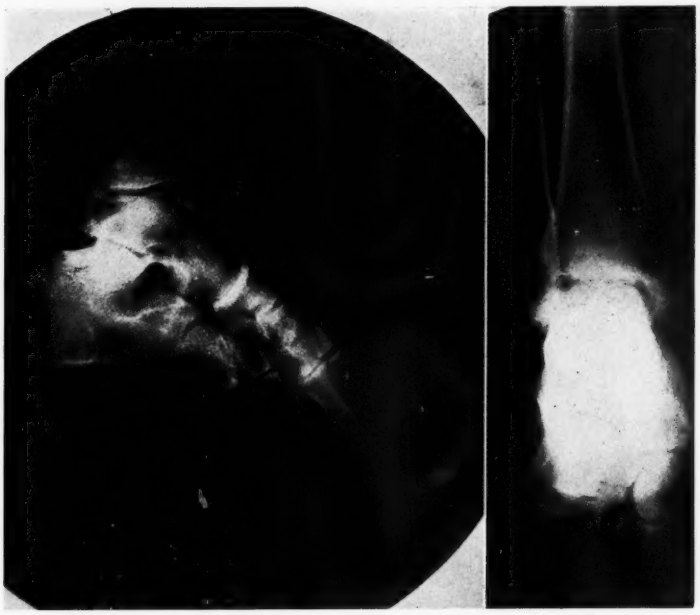

Fig. 3. Anteroposterior and lateral views of the left ankle, the site of the original metastasis, showing the lesions in the internal and external malleoli.

While it is true that basal-cell epithelioma is the usual tumor capable of cylindromatous changes in the stroma, endothelioma, especially the inter-fascicular type, may undergo such structural changes, and make it difficult to distinguish between the two lesions. Suteef (18) gives the essential differential characteristics as follows: Cylindromas of epithelial origin have their onset in childhood or young adult life, and are frequently familial or hereditary. Their exact etiology is unknown, but it may be from the sebaceous glandular epithelium. They are nodular, and have a predilection for the skin of the face, and hairy part of the head. Their course is benign. They may metastasize into the skin, but no glandular involvement occurs. Endothelial cylindroma, arising from the vascular endothelium, or that of the perivascular lymph spaces, may occur at any age, and is never hereditary. Any part of the cutis, including that and healing without scar tissue formation. The course is eventually malignant. The lymphatic glands become involved, though late in the course of the disease. Metastasis may occur in remote organs.

Clinically, endothelial tumors of the skin are characterized by spontaneous regression and new formation, and are relatively of slow growth. Unless stimulated by the trauma of surgical procedure, they metastasize rather later, and the lymph nodes are not affected as early as in carcinoma. On account of their infiltrating character, they are prone to recur at the site of excision much earlier than carcinoma. Suteef (18) is of the opinion that irradiation frequently aggravates rather than retards the course of the disease.

Gottheil (5), in 1907, reported the first authentic case of endothelioma of the skin. This tumor of the foot was regarded as a melanotic sarcoma because of its blackish color, until it was sectioned for microscopic

study. McDonagh (8), in 1912, reported five cases of nevo-xantho-endothelioma of the skin in children. Wise (12), in 1919, when the blood supply became occluded. This is a practical demonstration of Mallory's dictum (11), in which he directs

Fig. 4. Anteroposterior and lateral views of left ankle five weeks after first examination. Note that the lesions have extended to the os calcis, involving the tuber calcaneus and neck of the bone.

published an excellent protocol on the subject, and described two cases, one of endothelioma simplex in an adult, and another of nevo-xantho-endothelioma in a child. Jacoby and Grund (19), in 1930, reported the seventh case of nevo-xantho-endothelioma. These authors are of the opinion that the rarity of the disease is in a measure dependent on the recourse to clinical examination alone in the diagnosis of skin lesions, and lack of appreciation that extirpation of lesions for microscopic study is of paramount importance. In the cases described by them, the lesions were confused with multiple disseminated moles, urticaria pigmentosa, and syringo-cyst-adenomas, until they were biopsied. While Ewing (16) suggests that the origin of these tumors may be from neoplastic growth of endothelial cells of capillary nevi, the fact remains that their microscopic structure conformed to all of the characteristics of endothelioma. The yellowish color of the xantho-endotheliomas reported was due to lipoid histiocytosis of the endothelial cells attention to the phenomena attending defective blood supply in these lesions.

In 1920, Guttierrez (13) described a case in an adult female of numerous subcutaneous nodules of the external portion of the left mammary and pectoral areas, with no mammary involvement. One nodule was present below the right breast. This proved to be a rare case of lymphangioendothelioma of the skin. In spite of all treatment, which included radiation, nodules continued to form on the anterior abdominal wall, and a fatal outcome resulted.

Ewing found it difficult to eliminate Haslund's (4) case of endothelioma of the skin reported in 1906, which consisted of multiple tumors of the scalp, the history and course of which were typical, in which metastases occurred to the regional lymph nodes, and which proved fatal in 18 months. The type of cell was endothelial with intercellular fibrils. No epithelial characteristics were present. Yet, as Ewing states, such tumors, which are

localized to the scalp, are often of sebaceous gland origin.

Ewing (16) describes hemangio-endotheliomas of the skin, in which there is a preponderance of endothelial cells over new blood vessel formation. He accepts Winkler's (2) endothelial psammoma of the skin, derived from the endothelium of the neurilemma of the nerve fibers, and consisting of concentric masses of endothelial cells, which become calcified. This is analogous to endothelial psammoma of the dura, which was the pioneer endothelial tumor.

Furthermore, Ewing (16) calls attention to certain forms of fascial sarcoma of the extremities, which are derived from the endothelium of the capillaries. While he regards the cellular nevus as always melanomatous, some of the German authors, such as Kaufmann (17), contend that this may be of endothelial origin.

Mallory (11), who has devoted much study to the endothelioblastomas and their classification, states that morphologically the endothelial cell is not highly differentiated, and for this reason it stands out in marked contrast with those cells which are thus characterized when properly fixed and stained. He further asserts (7) that the endothelial cell is of mesoblastic origin, and all tumors derived from this cell, regardless of structure, should be termed endotheliomas.

Fig. 5. Radiographs of right ankle five weeks after initial examination, showing similar areas of osteolysis in the os calcaneus.

Without a doubt, the reticulo-endothelial system has manifold capacities for variable cell differentiation and tumor production, of which the last chapter has never been written. In view of the fact that this faculty has been amply demonstrated in different skin lesions of endothelial origin, a number of unquestionable cases of endothelioma cutis with similar pathologic findings have been described and reported, in recognition of the illuminating work of Zeit in differentiating these

tumors, in appreciation of the excellent protocol of Wise, and Mallory's treatment of the subject, it must be conceded that the lesion is a definite clinico-pathologic entity.

REPORT OF CASE

Mrs. E. A. J., housewife, white, aged 42 years, entered the Crisler Clinic on Oct. 5, 1931, with the complaint of "growths on left shoulder" of three months' duration.

Family History.—Irrelevant, with no history of malignancy in family.

Marital History.—The patient had been married 24 years, having had four husbands during this time, two children living and in good health, ages 22 and 17 years, and two miscarriages by last husband, three and nine years before first admission to clinic.

Menstrual History.—Onset of catamenia at 13 years of age, continuing regularly up to ten years previous to first observation. She had since suffered with irregularity, menorrhagia, and pre-menstrual pain.

Operation.—Right ovary and both tubes were removed with appendix, in 1927, two years prior to her first examination.

Past History.—The patient had had all of the usual juvenile diseases, with no injuries. She had entered the clinic two years before the present admission, complaining of colicky pains in the lower abdomen, bilateral, radiating to the small of the back, and aggravated by exercise. Menstruation had been regular since operation, but some menorrhagia as well as scanty flow had been noted. There was nausea and bloating after meals and occasional vomiting. Attacks of syncope had occurred. Pelvic examination had revealed an enlarged cystic left ovary, with uterus anteflexed. Cholecystograms showed a normally functioning gall bladder. Gastric analysis showed a total acidity of 17′, with a free hydrochloric acid of 13′. A mild albuminuria was found. No Wassermann was run at that time. The patient was given an abdominal support, and advised to return for further observation.

The pains in the lower abdomen had persisted during the interval since she was last seen. These were associated with soreness and stiffness in the lumbar region. The gaseous eructation had continued, and since the last spring she had had epistaxis two or three times a week. No skin lesions of any type had been noticed prior to the present efflorescences, and no moles of any character had been removed at any time.

Present Illness.—For one year, the patient had observed small buckshot-like nodules on different parts of the skin of the body and extremities, which appeared spontaneously, and which would regress and reform concurrently. These always appeared beneath the skin, and would gradually elevate to produce a tumefaction varying in color from a pinkish brown, or salmon tint, to that of a strawberry. She was mainly concerned with four reddish growths on the posterior aspect of the left shoulder, which were painful, and two of which showed ulceration. These had existed three months. Her home physician thought them to be a form of acne, or possibly a furunculosis. Primarily, only two nodules were present, which developed yellowish, necrotic centers; they were incised, but only a bloody serum was obtained. Almost immediately the adjacent lesions appeared. Six weeks before coming to the clinic, she had slipped and sprained her left ankle. This was strapped, but it remained tender and painful.

Physical Examination.—Well developed, fairly well nourished white female, presenting no evidence of cachexia. Four nodules varying in size from that of a pea to that of a lima bean were noted over the posterior aspect of the left shoulder (Fig. 1). The color varied from a pink to a strawberry, the larger ulcerated lesion being of the latter color. All were firm in consistency, two were painful to pressure, and the impression was that they were fleshy, and not of infectious etiology. Three smaller nodules, which were located above this group about the tip of the shoulder, were

more deeply situated in the sub-cutis, and felt like buckshot. There were only slight changes in the epidermis overlying these.

amination of the abdomen was negative for the presence of fluid, tumefaction, or tympanites, though some tenderness was

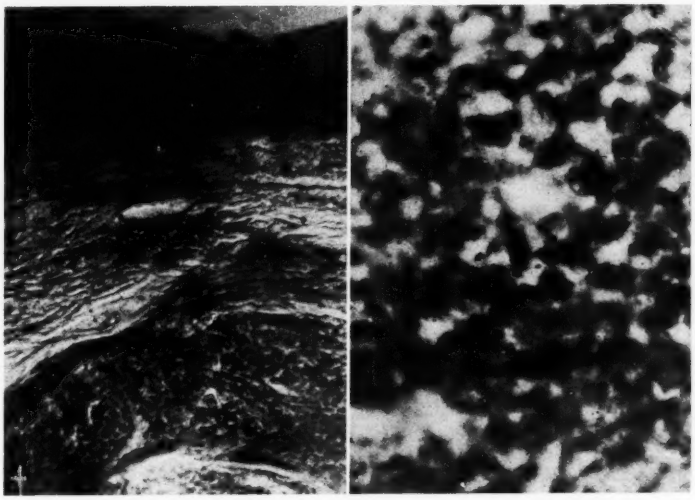

Fig. 6. Low and high power photomicrographs of skin nodule on anterior aspect of right thigh above the knee. In the low power view, note that the lesion develops a capsule as it approaches the normal overlying epidermis. In the high power view, the effect of irradiation on the cells is apparent. While the type of cell is identical with that in the first biopsy, the cytoplasm is swollen and hydropic, the nuclei are segmenting and disappearing, and there is a tendency to the fusion of cells into syncytial masses.

A large, tender gland was found in the left axilla, but no other enlarged superficial glands were palpated. In the skin of the right breast was another lesion, the size, shape, and color of which reminded one of a red mulberry. Many other nodules were well disseminated over the surface of the body, including the skin of the other shoulder, upper arms, scalp, thighs and legs, and the gluteal regions, 22 in all. Most of these were confined to the corium and sub-cutis.

The left ankle was not noticeably swollen, but some tenderness was elicited over the internal malleolus. The superficial and deep reflexes were normal. The eye, ear, nose, and throat examinations were essentially negative. The thyroid gland was not enlarged, and no circumscribed tumefaction was palpated within its substance. No adventitious sounds of any character were found in the chest. No tumor masses were felt within the parenchyma of either breast. The ex-

noted on deep pressure in the lower right quadrant. The lower margin of the liver descended only one finger's breadth below the costal margin. The spleen was not palpable. A pelvic examination revealed that the left ovary, which was cystic, had not increased in size since the previous observation. The uterus had remained anteflexed, and was of normal size. No tumor masses were found in the pelvis.

Laboratory Examinations.—Urinalysis was normal but for a mild albuminuria; leukocytes, 9,365; differential count—neutrophiles, mature forms 77 per cent, immature 2 per cent, lymphocytes 19 per cent, and eosinophils 2 per cent; red cells, 3,980,000; hemoglobin (Newcomer), 75 per cent, or 12.68 grams per 100 c.c.; color index, 0.9. No malarial plasmodia found. The Wassermann and Meinicke turbidity reactions were four plus positive. A biopsy was made of the skin nodule in the right breast.

Pathologic Report (Fig. 2).—*Parenchyma:*

Compact masses of rapidly proliferating mesenchymal cells, with distinct cellular membrane, clear or transparent cytoplasm, and pale vesicular nuclei, with multiple basophilic nucleoli. The arrangement was alveolar about dilated and congested, or collapsed, capillary blood vessels, and about lakes of red cells, where the anaplastic cells were in direct contact with the blood stream. In some areas the growth was intra-luminal. No pigmentation, no epithelial pearls, and no giant cells were present. An average of two to ten mitoses or prophases to the high power field was found. The mitotic figures stood out in extreme contrast in the clear cytoplasm of the cells, most of which were polyhedral in shape. Very distinct intercellular fibrils or processes were seen, and many of the cells seemed to taper into these. Definite hyalinosis of some of the cell masses was noted. The growth was confined to the corium and sub-cutis, and the overlying epidermis, other than showing thinning out of its layers, was normal with intact basement membrane. *Stroma:* Loose areolar connective tissue, supportive in character, and some fibrosis, though there was very little desmoplastic reaction. Some round-cell infiltration was present. The blood vessels were of the capillary type, dilated, and much engorged, but there was no capillary proliferation.

Fig. 7. Radiographs of left ankle four months after first examination. Note the stripping of the periosteum of the internal malleolus, also the advanced destruction of the os calcis, the involvement of the talus, and the moth-eaten appearance of the cuneiforms, cuboid, and the bases of the metatarsals.

Pathologic Diagnosis.—Malignant endothelioma of the skin.

Roentgen Examinations.—On account of the possibility of the skin lesions being metastatic from a deep-lying primary tumor, a complete roentgen study of all viscera was made. The chest was negative for any type of infiltration in either lung-field, and no mediastinal glands were found. The gastro-intestinal series revealed a gastrospasm, with relative fixation of the cecum without deformity, which was interpreted as the result of adhesions from the pelvic operation. No filling defects of any character were found in any part of the alimentary canal. Cholecystograms showed a normally functioning gall bladder. The liver shadow was of normal size, with smooth anterior margin. No-

glands were visualized in the abdomen. The splenic shadow was of normal size and position. A kidney, ureter, and bladder

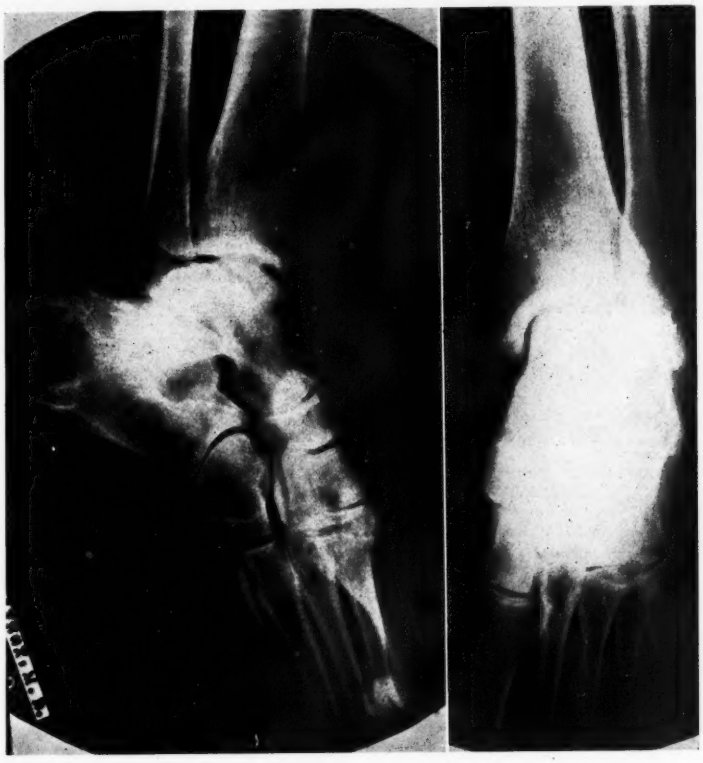

Fig. 8. Radiographs of right ankle four months after initial examination. The os calcaneus shows a sharply circumscribed area of osteoclasis, with a narrow delimiting zone of osteitis.

examination and bilateral pyelograms showed the kidneys to be of normal size, shape, and position, with no deformity of the pelves or calices; both ureters were in normal position.

Due to the tenderness and pain in the left ankle, radiographic study was indicated (Fig. 3). There was a definite rounded area of osteolysis 1.5 cm. in diameter in the internal malleolus, and a similar one of larger size in the external. The rarefaction was confined to the medulla of the bone in each instance, with indistinct margins. The overlying periosteum was not involved, and showed no reaction whatsoever. There was no expansion of the medullary cavity, and none of the soap-bubble, or trabeculated appearance characterizing benign giant-cell sarcoma, or osteitis fibrosa cystica secondary to hyperparathyroidism. Though this is one of the common sites for benign giant-cell sarcoma, the multiplicity of the lesions alone would exclude such a diagnosis. Due to this finding, the bones of the opposite ankle, spine, pelvis, and skull were studied for similar lesions. No definite erosion or rarefaction was found in any of the other bones at this time. There was no linear striation with increased density of any of the vertebral bodies that would suggest the presence of a primary hemangio-endothelioma of the spine, which has been described and reported by Ireland (24) and others. However, this tumor seldom metastasizes to the skin.

Since no other primary tumor was demonstrated, and since the lesions found

in the external and internal malleoli of the left ankle were distinctly metastatic in character, it was concluded that these as large as the one excised. In the right femoral trigone, a lymph node the size of a robin's egg was found.

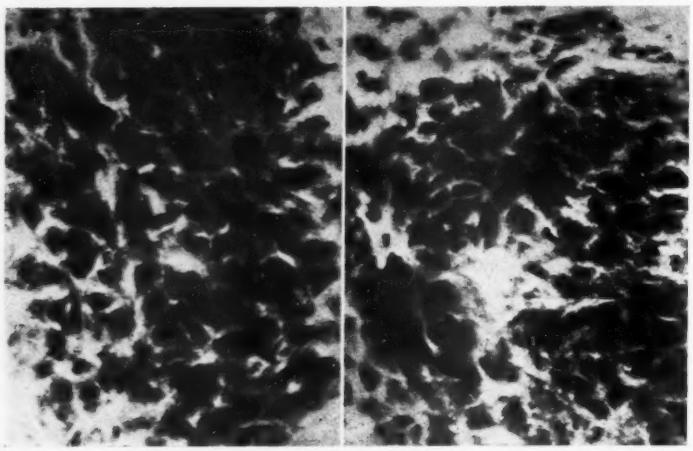

Fig. 9. High power photomicrographs of biopsy of internal malleolus of left ankle. While the type of cell is that found in the cutaneous lesions, the form is spherical or pavement-like, with fusion into syncytial masses. The cytoplasm is swollen and granular, with dropsical and poorly staining nuclei. Occasional mitoses are seen. These changes are no doubt secondary to irradiation and the edema of associated inflammation.

represented metastases from the endotheliomas of the skin. Associated with this condition was a positive Wassermann.

Treatment.—Nine of the most prominent skin nodules, including those on the left shoulder, were irradiated for diagnostic effect. Each lesion, well shielded with lead, received one S.E.D. Deep therapy at 200 K.V., with 0.5 mm. of copper, and 2 mm. of aluminum filtration was given to the left ankle through two lateral 10-cm. portals in a total depth dose of 600 r units. The patient was put on intensive mixed anti-syphilitic treatment, and advised to return in one month.

She returned to the clinic on Nov. 13, 1931, five weeks later. Several of the irradiated skin lesions, especially those on the left shoulder, had entirely disappeared, but there were 19 new ones diffusely distributed over the body surface. The left axillary lymphadenitis, which had received no radiation, had subsided. Adjacent to the site of the biopsy of the skin nodule in the right breast, there was another reddish papular excrescence almost

Radiographs of the left ankle (Fig. 4), which was definitely swollen, showed that the areas of rarefaction in the malleoli were more radiolucent and somewhat larger. There was absorption of all bony striæ, and no evidence of bone repair. The periosteum remained intact, and showed no reaction. The os calcaneus also showed a definite area of rarefaction in the tuber calcaneus, about two centimeters in diameter, and another of more advanced destruction in the neck of the bone adjacent to the articular surface for the cuboid.

The patient complained of pain in the right heel at this time. Radiographs of the right ankle and foot (Fig. 5) revealed similar areas of osteolysis in the calcaneus, but none in the malleoli. Roentgen examination of the spine, pelvis, and skull did not show any involvement. Small rounded areas of slight rarefaction in the vortex of the skull were interpreted as the shadows produced by the pacchionian bodies. The Wassermann remained four plus positive.

It was quite apparent that we were dealing with bone lesions, which were radioresistant, and which did not respond to specific therapy. There was definite extension of these to the bones of both feet. While these were characteristic of metastatic malignancy, other diseases of the bones, such as multiple myeloma and secondary osteitis fibrosa cystica, had to be considered. The bones of the ankle and foot are rare sites for the lesions of multiple myeloma. Repeated tests of the urine for Bence-Jones protein were negative. The blood calcium was 9 milligrams per 100 cubic centimeters. Orthopedic consultation resulted in the strong contention that the lesions were those of a chronic diffuse syphilitic osteomyelitis, and that the patient had not received sufficient antisyphilitic treatment.

The patient was placed in the hospital, and intensive specific therapy again instituted. The right femoral lymph node continued to enlarge, and became painful. This was excised, following irradiation. The pathologic report was endothelioma, probably metastatic, invading the sinuses and follicles of the gland. The patient returned home in one month apparently improved. The anti-syphilitic regimen of treatment was continued, and the report from her home physician was encouraging. She had gained in strength, but the left ankle had become more swollen, and the pain almost unbearable. One skin nodule, situated above the right knee on the anterior aspect of the thigh, showed progressive enlargement.

She re-entered the clinic on Feb. 9, 1932, three months after the last observation. Her general appearance was cachectic. The skin was of icteroid tint, and there was much loss of weight. The patient was hospitalized and transfused. Following irradiation, the skin nodule above the right knee was excised. This growth was the size of a marble with reddish overlying skin. It was apparently well encapsulated, and cells could be brushed from its meaty, translucent surface only with the greatest difficulty.

Pathologic Report (Fig. 6).—*Parenchyma:* Diffuse growth of the identical type of cell found in the original biopsy; cytoplasm clear with small centrically placed vesicular nuclei and multiple nucleoli. No perivascular arrangement was found. Most of the cells were polyhedral in shape, but many were ovoid or spherical, or appeared swollen with granular cytoplasm, and hydropic, faintly staining nuclei, and even fused into syncytial masses, probably as a result of the radiation. The anaplasia was well marked, with two to four mitoses to the high power field. Much infiltration with round cells was present. No pigmentation of any character was demonstrated in any of the cells. The overlying epidermis, while it was thinned out due to pressure, was normal with intact basement membrane. *Stroma:* Loose areolar connective tissue, with some fibrosis. Fine reticular fibrils were noted between many of the cell masses. There were many capillary blood vessels, dilated and injected, but there was no hyperplasia of these.

Pathologic Diagnosis.—Malignant endothelioma of the skin.

Roentgen examination of the left ankle (Fig. 7), which was tremendously swollen, red, and edematous, showed the styloid process of the fibula totally destroyed on its posterior aspect, and the periosteum stripped up. The internal malleolus was rarefied throughout except at its tip, and the periosteum was floating. The calcaneus showed mottling and rarefaction throughout its length, more advanced in the tuberosity and neck of the bone. There was also osteolysis of the talus on its volar surface. A moth-eaten, diffuse rarefaction was seen in the cuneiforms, cuboid, and the bases of the metatarsals. The right heel (Fig. 8), which continued to be painful, showed a circular area of osteoclasis about 2.5 cm. in diameter in the calcaneus, with a delimiting zone of osteitis. There was also rarefaction in the neck of the calcaneus, and an irregular mottling in the internal cuneiform. Decalcification was noted in the malleoli.

The Wassermann was again reported four plus positive.

The patient returned home, and continued to grow weaker. Three months later, May 22, 1932, she re-entered the hospital. Two transfusions were given. At this time it was discovered that a tumor the size of an English walnut had developed in the parenchyma of the right breast. This, along with a small nodule in the skin of the left thigh, was removed. The pathologic reports described the same type of neoplastic cell found in the microscopic study of other lesions, or malignant endothelioma. The patient gained a few pounds in weight, but remained very much anemic, with icteroid skin. Liver extract and calcium gluconate were given.

On Aug. 20, 1932, a biopsy of the internal malleolus of the left ankle was performed. This was readily done under local anesthesia. The bony structure of the process had been entirely destroyed, and the growth was very accessible. Pathologic examination (Fig. 9) disclosed the precise type of cell described in the cutaneous lesions, though many of the cells were spherical or pavement-like with dropsical nuclei, and stained poorly. No giant cells or epithelial structures were present. There was marked infiltration with round cells. A detailed search with special staining methods did not reveal any trace of melanin-like pigment. The growth had invaded the venous channels.

Fig. 10. Radiographs of left ankle at time of biopsy of internal malleolus, ten and one-half months after primary examination. There is a pathologic fracture of the fibula above the external malleolus, and advanced osteolysis of all bony structures.

This significant finding furnished conclusive proof that the bone lesions were neoplastic in nature, and metastatic from the tumors primary in the skin. The persistently positive Wassermann indicated an antecedent syphilitic infection of long standing.

Radiographic examination of the ankles at this time showed that in the left ankle (Fig. 10) there was a marked osteolysis of the internal malleolus as well as in the external, with a pathologic fracture of the fibula above the malleolus. All of the bones of the foot were more or less involved by the same process, but all joint surfaces remained intact.

The right ankle (Fig. 11) showed extension of the circular area of erosion in the os calcis, also a similar circular area of rarefaction 1.5 cm. in diameter in the neck of the talus, and generalized decalcification and rarefaction in the other bones of the tarsus, especially the cuboid. The bases of all the metatarsals were involved. Definite osteolysis was observed in both malleoli.

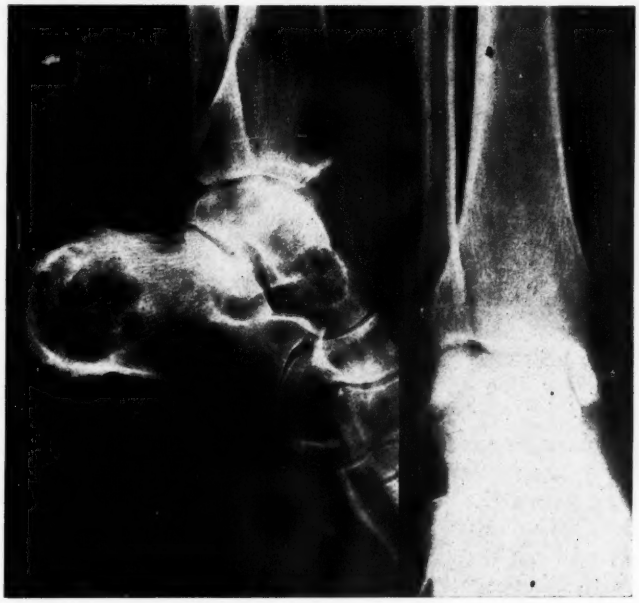

Fig. 11. Radiographs of right ankle made at time of biopsy of left internal malleolus. There are areas of rarefaction in practically all of the bones. The circular area of erosion in the os calcis shows definite extension.

The patient complained of excruciating pain in the right heel as well as in the left ankle. Deep therapy was applied to both ankles on Aug. 24. The irradiation was repeated on Oct. 8, and again on Dec. 5. Pain persisted, and the destruction of bone continued, although a total depth dose of three S.E.D. had been delivered to either ankle and foot. She left the hospital with no relief.

On Jan. 19, 1933, the patient again entered the hospital, mainly for the relief of pain. Cachexia was marked. There was a large gland in the left femoral region, and she was suffering from distress in the left lower quadrant, radiating to the back. Radiographs of the pelvis showed destruction of the upper half of the left wing of the sacrum. Deep therapy was given over the pelvis through anterior and posterior portals for the mitigation of symptoms. The following March, since opiates did not give rest, the left leg was amputated at the knee. Yet, she complained there was agonizing pain in the left ankle.

On June 22, 1933, one year and eight months from the time the patient was first seen, or two years and eight months from the time skin nodules first appeared, a lethal exitus occurred. On the day previous, a pulmonary hemorrhage ensued, which lasted until death. Every joint had become swollen. A large tumefaction, which presented above the right knee, the site of excision of a skin nodule, ruptured three weeks before death, and drained an odorless pus. No autopsy was obtained.

COMMENT

This case is reported because it com-

prises several unusual features. First, endotheliomas of the skin are very rare, and their occurrence has been repeatedly disputed. Virchow has aptly stated that an organ, often the site of metastatic lesions, is seldom the site of primary ones. Second, the multiplicity and wide distribution of the lesions is interesting. These fulfilled all of the requirements of primary malignancy in that each lesion was distinct, presented a definite picture of malignancy, and one being the metastasis from another was improbable, as they appeared simultaneously, and were remotely separated. Third, the bone metastases are remarkable for their time of appearance and initial location. Their rather early occurrence was in all probability due to improper surgical intervention. They were characteristically secondary lesions in that the rarefaction began in the medullary cavity of the bone, and reached the periosteum only by extension. They were all of the osteoclastic type, with no reaction in the bony structure with the exception of narrow zones of osteitis. The primary metastasis occurred at the site of trauma, the injured left ankle, which evidently furnished a point of lowered resistance, the congestion and stasis producing a pabulum favorable to the growth of tumor emboli. However, the bones of the opposite ankle became involved before metastases were found in those of the trunk. Ordinarily, metastatic lesions rarely affect the extremities below the elbows or knees, which are common sites for infectious emboli. Moreover, the growth is usually found at the point of entrance of the nutrient foramina, or of exit of the veins. In this case, the initial metastasis appearing in the malleoli was phenomenal. Fourth, the association of a concomitant chronic syphilitic infection, as the history and a persistently positive Wassermann would indicate, is a coincidence. As it is well known that the reticulo-endothelial system is very susceptible to, and reacts to various, acute and chronic infections, presumably, this may have been the exciting inflammatory agent in producing the endothelial hyperplasia.

The diagnosis was based on the clinical observation of concurrent, voluntary regression and new formation of pinkish to red, papular or nodular skin lesions, originating in the corium and sub-cutis, and diffusely disseminated over the surface of the body, which condition had existed for a period of one year in a relatively well nourished patient. The tumefactions were present where no sebaceous glands are found. The remote possibility of the lesions being metastases from a deep lying primary tumor was excluded by thorough examination, and the fact that the regression of cutaneous nodules is not representative of a metastatic process. The excision or incision of one of the growths was followed by early recurrence, or the appearance of other lesions adjacent to the site of operation. These observations are almost characteristic of endothelioma cutis. While the primary tumors responded to single erythema doses of radiation, their metastases to the bones were definitely radioresistant.

Pathologically, the cut surface of the tumors was translucent, and the cells were brushed from the stroma only with difficulty. After fixation there was no retraction of the cell masses, which occurs in epithelioma. The type of cell in all unradiated specimens was typically endothelial. These were polyhedral or spindle-shaped, with clear, stainless cytoplasm with small vesicular nuclei, some of which contained many minute nucleoli. While the direct contact of the anaplastic cells with the blood stream is not diagnostic, the arrangement in compact layers, or alveoli, with definite intercellular processes or fibrils is characteristic. In the edematous and irradiated foci, such as the left ankle, the cells reverted to the pavement type, many of which were swollen to spheroidal form, and of considerable dimensions, which agrees with Ewing's (16) observations.

The patient had never had a pigmented mole prior to the appearance of the cutaneous nodules, and no moles had been removed at any time. Becker (25) has

shown that melanoma arising from a pigmented nevus has its origin in the melanoblastic cells at the epidermo-dermal junction, and not in deep lying nevus cells. The lesions in question originated in the deeper layers of the dermis and sub-cutis, and became encapsulated as they approached the normal epidermis. No pigmentation of any character was demonstrated in any of the biopsied or surgical specimens. While the quiescent or adult white mulberry melanotic nevi may not show melanin pigment, and while the degree of pigmentation is not an index of malignancy, it can usually be found in varying amounts by diligent search, especially in malignant melanoma. Metastasis occurs simultaneously with malignant change in melanomas, and while the secondary lesions are common in the skin and liver, they are strictly progressive, and show none of the regressive changes manifested in the cutaneous tumors described, nor do they respond to single erythema doses of radiation. Metastasis to the bones is not often found in melanoepithelioma. The flat bones are more often affected than the long ones. Sutherland (23), in the analysis of the cases which have come under his observation, has arrived at a similar conclusion. Copeland (20) found only three instances of metastatic growth in bones in 169 cases.

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RADIOLOGIC STUDY OF THE DEVELOPMENT OF THE SPINE AND PATHOLOGIC CHANGES OF THE INTERVERTEBRAL DISC[1]

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ONLY in the past few years has any intensive clinical attention been paid to that highly specialized and very important structure, the intervertebral disc. Although it was originally described by Vesalius, in 1555, and an accurate description of its embryology and anatomy made by Von Luschka, in 1858, it was not until 1927 that Schmorl, of Dresden, made the first clinical and pathologic studies in which he observed the frequent prolapses of the nucleus pulposus into the adjacent vertebral bodies.

Before the publication of Schmorl's painstaking work, the intervertebral disc was generally regarded as a more or less unimportant plate of fibro-cartilage. Now that we have become cognizant with this organ as it really is, we have been able to explain a great number of hitherto inexplicable problems in relation to affections of the spine.

To understand the anatomy and function of the disc it is necessary to know something of its development, which will be discussed in a brief survey of the development of the spine as a whole.

THE DEVELOPMENT OF THE SPINE

There is a certain amount of controversy between different authors on the development of the spine. Remak and Bardeen say that mesenchymal cells arrange themselves in segments about the notochord in accordance with the primitive segmentation of the embryo. These form the provertebræ which are marked off by the intersegmental artery. Now, each is divided into a dark caudal and a light cephalic half. Union of adjacent halves takes place, thus forming the definitive vertebræ.

Williams disagrees with this theory, stating that following the arrangement of mesenchyma there is no formation of provertebræ. According to him, definitive vertebræ are formed merely by differential growth. Very little differentiation takes place in the intervertebral area, which explains its dense appearance.

Keyes and Compere make the most comprehensive explanation, in which they more or less combine the two above-mentioned theories. According to them, the mesenchyma of the sclerotome migrates about the notochord. Segmentation occurs, each segment being composed of a light cephalic half and a dark caudal half and is separated from its neighbor by the intersegmental artery. The cells nearest the artery receive more nutrition and differentiate more rapidly. Finally, these two portions of adjacent segments merge and become the anlage of the vertebral body. The cephalic portion of the caudal mass, being farthest removed from the source of nutrition, remains undifferentiated and is the anlage of the disc. In this connection, it is interesting to note that the disc remains avascular throughout life. As the vertebral portion develops, pressure is exerted on the notochord cells, extruding them into the disc, where they undergo mucoid degeneration and form the nucleus pulposus. At ten weeks the vertebral bodies are composed of cartilage cells, and ossification centers are present. The site of the notochord may be seen as a mucoid streak in the bodies. The disc is composed of the enlarging nucleus pulposus, surrounded by fibro-cartilage which is the annulus fibrosus. After birth, the notochord cells have disappeared and growth of the nucleus pulposus is chiefly by proliferation of the fibrous element. Occasionally, however, remnants of notochord cells are found in the adult disc. As the child becomes older there is greater and

[1] Read by B. R. Mooney, M.D., before the Radiological Society of North America, at the Twentieth Annual Meeting in Memphis, Tenn., Dec. 3–7, 1934.

greater ingrowth of fibrous tissue into the gelatinous nucleus, until, at the age of from 8 to 12 years, it is composed almost completely of fibro-cartilage with an abundant gelatinous matrix. This progression continues throughout life until we see the senile nucleus, composed of dense fibro-cartilage with little or no gelatinous material. However, these changes will be discussed later.

Fig. 1.

Fig. 2.

Fig. 1. Six months' fetus (autopsy specimen). Note dense ossification nucleus.

Fig. 2. Full term fetus (autopsy specimen). Note excavation anteriorly, due to the central plate not extending as far anteriorly as the upper and lower plates (enlarged).

Hanson, in an article on "The Development of the Spine as Seen in Skiagrams," satisfactorily explains some peculiar appearances which were previously not exactly understood. Up to the fourth month of fetal life nothing unusual is noted. After this period the body is composed of two plates of dense calcified cartilage, between which is a lighter zone which does not extend as far anteriorly. In this central zone, cartilage is being absorbed and ossification begins as is evidenced by a dense nucleus in the center. After the second year the vertebræ usually have a homogeneous appearance, the spongy bone having extended to

both the upper and lower plates. The excavation anteriorly, caused by the overlapping of the outside plates, has disappeared after two years, except in the lower five to seven dorsal and one to two lumbar bodies. Occasionally, however, it persists as a rounded indentation or a hole just behind the anterior surface of the body.

Slit formations in the bodies of the vertebræ have been seen by innumerable observers. These were first described by Hahn, in 1922, who said that they were due to nutritional foramina. He added that they were seen only in the short period of adolescence, associated with a greatly increased blood supply and development of

Fig. 3. Man 37 years of age. Note persistence of slits in the bodies.

Fig. 4. Boy 14 years of age. Staircase-like appearance of the bodies.

Fig. 5.

Fig. 6.

Fig. 5. Block vertebræ. Note congenital absence of discs. Fusion of second and third cervical vertebræ, and of fifth, sixth, and seventh cervical vertebræ.
Fig. 6. Block vertebræ (lumbar).

the epiphyses. Köhler agreed with this theory.

Hanson, investigating this occurrence anatomically and radiographically, stated that Hahn's conclusions were inadequate and partly erroneous. His dissections on these vertebræ revealed a U-shaped venous channel, lined with a single layer of epithelium. The limbs of this "U" faced posteriorly, and could be probed as far back as the vertebral canal. Microscopically, these channels were filled with blood and bone marrow. Again, refuting him, Hanson states that in a large series of cases the greatest number of slit vertebræ were present in spines of children from 3 to 7 years old. Development of the epiphyses, he points out, occurs in individuals aged from 11 to 15 years. Supporting Hanson, who has seen these at various ages up to 35 years, we have seen these slits in the vertebræ of a man 37 years of age. The disappearance of these, radiographically, is in all probability due to the greater density of the cortical bone as the individual becomes older.

Another radiologic appearance not uncommonly seen in children is a staircase-like formation on the anterior edges of the vertebral bodies. Keyes and Compere believe this is due to a disturbance in the epiphyseal ring which is derived from the cartilage plates. They cite a case which, when x-rayed eight years later, revealed a typical juvenile kyphosis, with herniation of the nucleus pulposus into the vertebral bodies. Our case shows no evidence of kyphosis.

Fig. 7. Calcification of nucleus pulposus. Note compression fracture caused by minor injury.

Fig. 8. Umbilication of the discs. Note rupture into the body of a lumbar vertebræ (arrow).

PATHOLOGY OF THE INTERVERTEBRAL DISC

The simplest way to understand the intervertebral disc is to regard it as a rudimentary joint. The cartilagenous endplates are comparable to the articular cartilages—the annulus fibrosus to the fibrous capsule and the nucleus pulposus to the joint cavity.

The adult disc is composed of the following structures, in order, from the surface of the vertebra to the center:

(1) Thin cortical bone of the body of the vertebra—compact over the nucleus pulposus, and porous at the periphery.

(2) Cartilagenous plate—formed of a thin layer of hyaline cartilage which ends

abruptly anteriorly and laterally by abutting the bony epiphyseal ring, which is derived from it.

sectioning a fresh intervertebral disc. As the annulus fibrosus is cut, the nucleus pulposus promptly bulges into the incision.

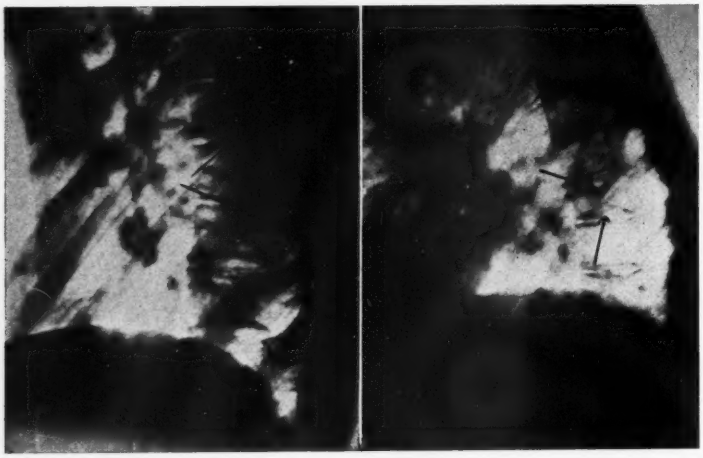

Fig. 9. Juvenile kyphosis in a youth aged 21 years. Note narrowing of the discs and multiple ruptures of the nucleus pulposus. Beginning osteo-arthritis of upper bodies.

Fig. 10. Senile osteoporosis and kyphosis. Herniation of upper and lower discs through a body (arrow), possibly due to persistent notochord.

(3) The annulus fibrosus—a dense fibrocartilagenous envelope, which forms a strong and elastic container for the nucleus pulposus.

(4) The nucleus pulposus itself—a fibrogelatinous incompressible mass.

It must be noted that the adult disc contains neither blood vessels nor nerves, its nutrition being supplied by lymph. The bony surface of the spongy bone shows minute perforations which allow nourishment to the disc by diffusion. Jung, after very careful investigation, was able to demonstrate nerves in the anterior and lateral ligaments only.

The function of the disc is to transmit static and muscular forces from one vertebral body to another, and on it depends the axis of motion of the spine. The most important portion of the disc—the nucleus pulposus—is subject to the usual laws of fluids; it is incompressible, and its function depends on the integrity of its confining structures, the annulus fibrosus and cartilage end-plates. That it is under tension from these structures is readily demonstrated by

The pressure of the nucleus pulposus after cutting away the annulus fibrosus is 1.8 mm. of mercury. The pressure required to reduce this expansion is 32.2 pounds.

Radiologically, in most cases, conclusions in regard to the condition of the disc must be drawn from the width of the intervertebral space and the condition of the borders of the adjacent vertebral bodies.

There is such a close relationship between all the components of the disc that I think the pathologic changes will be more clearly understood if such changes are discussed separately under each structure.

1. *Congenital absence of the disc.* This is not to be confused with calcification or destruction, which are described below.

2. *Pathologic conditions of the nucleus pulposus and annulus fibrosus.* Any condition that allows leakage of the nuclear material gradually results in partial or complete destruction of the disc. As a result of this leakage and destruction, the vertebral bodies rub together, causing sclerosis, osteo-arthritis, and lipping.

(*a*) *Retropulsion or antipulsion.* Due to

a tear of the annulus fibrosus, there may be a rupture of the nucleus pulposus, *e.g.*, posteriorily into the vertebral canal. Such a calamity would probably cause paraplegia. We have seen one such case.

(*b*) *Lateral shift.* This is seen in cases of scoliosis, and although it may not be the underlying cause it may explain the great difficulty in its correction. In such a condition the nucleus is situated at the convexity of the curve.

(*c*) *Calcification.* This was first seen, in 1858, by Luschka in an anatomic preparation; but Calvé and Gallard, in 1922, were the first to describe it in a radiograph of a living subject. The etiology is indefinite but infection (Köhler), disturbed calcium metabolism, trauma, senility, etc., have been suggested as causes.

(*d*) *Infiltration by other tissues—fibrous tissue, bone, and blood vessels.* Fibrous tissue is, of course, the most common and is characterized radiographically by a narrow intervertebral space varying in degree. Such changes accompany old age, or follow trauma as a healing process. Complete ossification of a disc may occur. Ossification of a congenitally small disc may give the picture of congenital block vertebræ.

(*e*) *Dehydration.* Puschel has estimated the water content of the nucleus pulposus for different age groups as follows: full term, 88 per cent; 18 years, 80 per cent; 77 years, 69 per cent. Thus dehydration accompanies senility. However, if there has been any leakage of nuclear material due to any one of several causes, this dehydration is greatly increased.

3. *Pathological conditions of the cartilaginous end-plates.*

(*a*) The prolapse of the nucleus pulposus, because of its expansile power, is due to congenital defects or weakness of the cartilaginous plates. The latter condition, that is, weakness of the cartilaginous plates, is evidenced radiologically by the presence of smooth excavations in the vertebral bodies, and is described by Smith as umbilication of the disc. This condition is also seen in all softening diseases of the bodies of the vertebræ, *viz.*, osteoporosis, tuberculosis, etc., and will be described under diseases of the vertebral body. The former, that is, congential defects in the cartilaginous end-plates, is due to congenital fissures or cracks in the plate, allowing leakage of the nuclear material into the spongiosa of the bodies. When this occurs, a reaction in the bone is set up, resulting in the formation of a cartilaginous nodule eventually surrounded by a wall of sclerosed bone. Radiologically, this is recognized by a narrowing of the intervertebral space, and, after sufficient time has elpased, by the presence of Schmorl's knots in the vertebral bodies. Both these conditions of the cartilaginous end-plates are probably etiologic factors in epiphysitis, dorsalis juveniles (juvenile kyphosis), and osteo-arthritis, as was explained above.

(*b*) *Chronic trauma.* Schmorl found different degrees of prolapse of the nucleus pulposus in 38 per cent of routine spinal autopsies. He attaches little significance to these findings, but investigated the histories of only a few of the cases. He states, however, that continual, every-day trauma will cause minute cracks in the cartilage plates, consequent dehydration, destruction of the disc, and more wear and tear on the vertebral margins, resulting in osteo-arthritis.

(*c*) *Acute trauma.* Destruction of the disc is frequently associated with compression fracture of the vertebra. The cartilage plates, however, are surprisingly strong and may suffer little or no damage. In connection with this, Schmorl has seen numerous cases showing no injury to the discs at the time of accident, but years later Schmorl's knots were present in distal vertebræ. This demonstrated that injury to these discs had occurred.

(*d*) *Fibrillation.* Schmorl has frequently come across this condition, and likens it to the same condition affecting the cartilages of the knee and hip joint.

(*e*) Diseases of the disc, such as acute osteomyelitis and tuberculosis, are secondary to diseases of the vertebral bodies. Schmorl has not been able to demonstrate any primary infection in the intervertebral disc.

4. *Pathologic conditions of the vertebral bodies.* Any disease that causes softening of the vertebral body results in prolapses of the intervertebral disc into the body. The vertebræ become bi-concave like those of a fish. Finally, the cartilage plate ruptures because of pressure of the nucleus pulposus, and the disc is eventually destroyed. Examples of such diseases are osteomalacia, generalized osteitis fibrosa and Paget's, senile osteoporosis, tuberculosis and neoplasms, benign and malignant.

In conclusion, we would like to add that Keyes and Compere have made some very interesting experimental studies. By various means, such as puncturing the annulus fibrosus to allow nuclear material to escape, they have produced prolapse of the nucleus pulposus into the adjacent bodies, destruction of the disc, lipping of the bodies, and osteo-arthritis.

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CASE REPORTS AND NEW DEVICES

A SIMPLE METHOD OF LOCATING LOST RADIUM IN AN EMERGENCY[1]

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Despite the great care exercised in the handling and storing of radium it is frequently misplaced, and, due to its small size, may be difficult to locate. If by chance it is thrown into the trash, it usually finds its way to the ash pile by way of the incinerator. Terrestial temperatures do not affect the radio-activity of the element but often destroy the containers completely, thereby allowing the radium to diffuse into the surrounding ashes. In this state the only practical method of detecting its presence is by means of the ionization which it produces in the surrounding air. Since the element may be recovered, except for an insignificant loss, it is of first importance that the ashes containing it should be separated and saved.

The purpose of this article is to describe a simple method of locating misplaced radium, in the case of such an emergency, by the use of a condenser type r-meter and an easily constructed ionization chamber.

The problem which is presented is that of measuring the dose, or the amount of ionization of the air. The magnitude of the gamma radiation from 50 mg. of element filtered by 2 mm. of brass is of the order of 5 r per minute at a distance of 1 centimeter. As the chambers usually supplied with condenser type r-meters produce a full-scale deflection of 25 r, it would take about two minutes to get a good deflection at this distance. By applying the inverse square law it is found that at a distance of one meter the intensity is only one ten-thousandth of that at one centimeter. This means that the time required to get the same reading would be ten thousand times as long, or about 300 hours. Were the insulation of the instrument perfect it would be possible to locate the radium with the r-meter directly; however, this would be a very tiresome procedure.

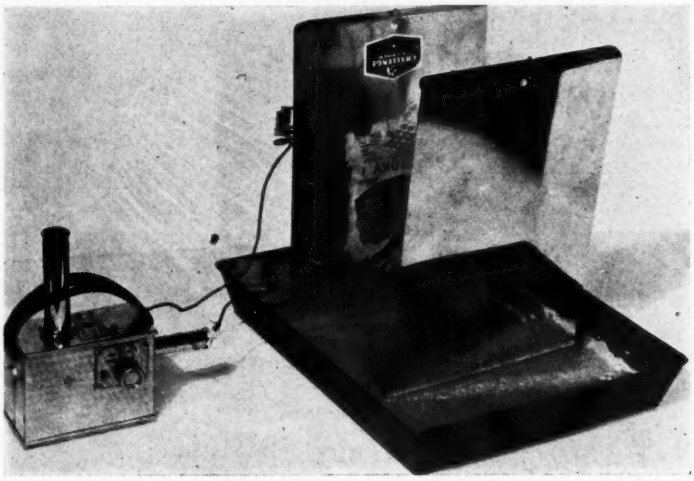

Fig. 1. A simply constructed chamber by the use of which 50 mg. of radium may be detected at a distance of 25 feet.

The simplest way to increase the sensitivity of these instruments is to enlarge the effective volume of the ionization chamber. Since the r is defined as the quantity of radiation which frees a certain charge per cubic centimeter of air, it is necessary only to increase the volume utilized in the same proportion as the desired increase in sensitivity. To change the time required from 300 hours to 2 minutes, a ratio of ten thousand to one, the volume must be changed from the popular one cubic centimeter chamber to a 10,000 cubic centimeter chamber, or should be made a cube with approximately 15 centimeters on a side.

The accompanying photograph (Fig. 1) shows a simply constructed chamber which can be set up in a very short time in case of an emergency, and which proves very satisfactory. When it is connected to a Victoreen condenser type r-meter it will detect the presence of 50 mg. of radium at a distance of 20 to 25 feet.

[1] Accepted for publication March 25, 1935.

It is constructed of two aluminum cookie sheets and a bread pan, and is insulated with sulphur. The cookie sheets (20 by 30 cm.) are suspended over the pan in the position shown and so as not to touch the bottom. Melted sulphur is then poured in through a gauze strainer, making an excellent insulator and mechanical support. One plate is connected to the frame of the r-meter by means of one of the screws which hold the handle. The other plate, or cookie sheet, is connected to the terminal in the middle of the receptacle which normally holds the thimble chamber and condenser. The wire leading to this terminal is insulated by a sulphur bushing which is made by placing a wire in a test tube and pouring in melted sulphur. When the sulphur has hardened the end of the tube is broken off and one end of the wire is coiled into a small spring which can be made to fit around the center terminal in the r-meter chamber receptacle. After the sulphur bushing is placed in the r-meter and the connection is made, the outside of the projecting portion is taped to the meter. (One should be careful to avoid producing a short circuit through the adhesive tape.)

The meter is then ready for use and may be charged to the zero position by turning the charging wheel in the same manner as it is ordinarily used. It will be noticed that the string drifts slowly across the field due to insulation leakage and the small amount of ionization in the air. This leakage rate can be determined with a stop watch. Any increase over the normal rate denotes the presence of radium or some other source of ionization. With the chamber shown, 50 mg. was easily detected at a distance of 25 feet.

If radium is located in the ashes they should be tested by the wheelbarrow-full until the "hot" load is found. This should then be tested by the shovel-full until the radio-active portion is found. If the container has not been destroyed, it should be found intact, but if it has melted, it is usually possible to find one or two clinkers which contain the majority of the element.

RIGHT-SIDED AORTA

REPORT OF TWO CASES

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That the condition of right-sided aorta is rare is illustrated by the fact that Biedermann[1] reports 12 cases in a series of 20,000 autopsies, and Holzapfel could find only 21 cases of right-sided aorta in a search of the literature between the years 1766 and 1891. Since then several cases have been reported.

Fig. 1. Shows the knob of the aorta on the right side of the vertebral column instead of on the left. The heart is in the normal position.

The condition should not be confused with transposition of the aorta, in which the aorta arises from the right ventricle and the pulmonary artery from the left. The origin of the aorta is normal but the course is not. It may be accompanied by perforation of the septa, patent ductus Botallo, transposition of the aorta and pulmonary artery, or abnormalities in the branches of the great vessels. Cases are reported in which there is a defect in the ventricular septum immediately below the origin of the aorta so that the vessel arises from both ventricles. The aorta is then broadened and the pulmonary artery narrowed. In these cases the diagnosis was made at autopsy.[2]

The condition may occur alone in perfectly healthy persons and need not cause symptoms, or it may be an accidental finding, as it was in both our cases. The most prominent symptom of these was difficulty in swallowing, due to an abnormal position or narrowing of the esophagus which is sometimes pressed upon by the aorta or the left subclavian artery. Renander[3] reported a case which was fluoroscoped because of difficulty in swallowing. The findings were a right-sided aorta and a rather marked dis-

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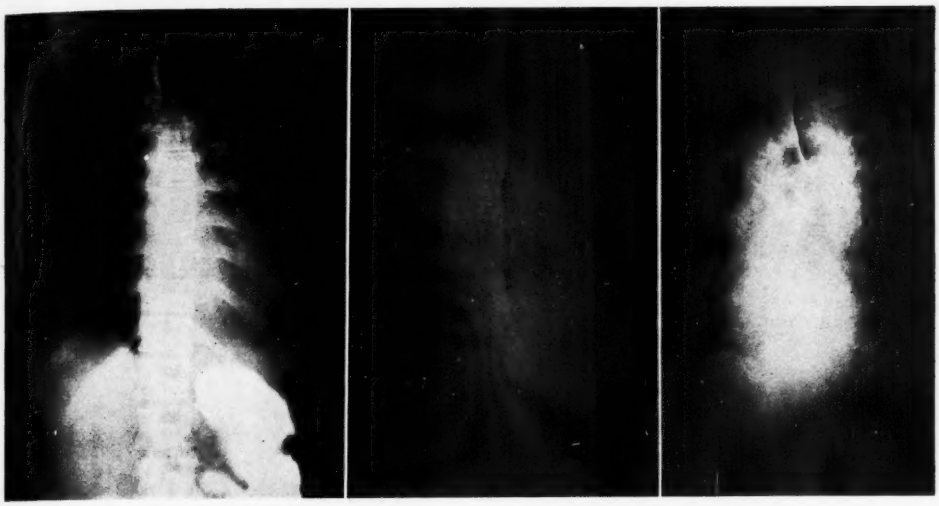

Fig. 2. Bucky film showing the knob of the aorta on the right side. The descending aorta and thoracic aorta run to the right of the dorsal vertebræ as far as the twelfth, where they turn toward the left.
Fig. 3. Right oblique position showing absence of the knob of the aorta and of the aortic depression in the esophagus.
Fig. 4. Left oblique position showing the knob of the aorta and the aortic depression in the esophagus.

Fig. 5. Showing the knob of the aorta on the right side of the vertebral column instead of on the left.
Fig. 6. Right oblique position showing absence of the knob of the aorta and of the aortic depression in the esophagus.
Fig. 7. Left oblique position showing the knob of the aorta and the aortic depression in the esophagus.

placement of the esophagus to the left and forward.

Roentgen Findings.—The knob of the aorta is not present in its usual left position. To the right side of the vertebræ, at the same level, an oval shadow which represents the knob of the right-sided aorta is seen, which pulsates on fluoroscopic examination. In the right oblique position the knob is not seen but it appears in the left oblique position. The aortic depression in the esophagus is also seen in the left oblique and not in the right oblique position, which is the normal. This depression may be normal in depth or it may be exaggerated to any degree by a further abnormal position of the aorta or left subclavian artery. The esophagus may be displaced to a marked degree, as shown in Renander's case.

The following cases are presented because of the extreme rarity and great interest of the con-

dition. One case was of the pure type while the other was accompanied by another abnormality.

Case 1. E. M., colored female, aged 30, entered the Morrisania City Hospital Dec. 7, 1932, complaining of attacks of fainting associated with palpitation and dyspnea on slight exertion. These conditions had been present for the past ten years but of late they had become more frequent, occurring daily. When a child she was told she had heart trouble. As far back as she can remember she has become dyspneic upon slight exertion. Physical examination showed a systolic thrill over the precordium. Rough high-pitched systolic and diastolic murmurs were present over the entire precordium. These signs were interpreted as being due to congenital heart disease of the nature of a septum defect. The electrocardiogram showed evidence of some myocardial disturbance in both auricles and ventricles, such as is found in congenital heart disease and in conditions in which right heart pathology is present.

Radiographic and fluoroscopic examination of the heart (Fig. 1) showed an absence of the knob of the aorta in its usual left position. Immediately below the inner end of the right clavicle an oval pulsating shadow was seen, adjacent to and continuous with the superior mediastinal shadow. This was interpreted as the knob of a right-sided aorta. A film (Fig. 2) made with the Bucky diaphragm in order to demonstrate the descending aorta showed that this vessel ran at the right of the dorsal vertebræ as far as the upper border of the twelfth, where it turned toward the left. Fluoroscopic examination and a film made in the right oblique position (Fig. 3) did not show the knob of the aorta nor did they show the depression which the aorta usually makes in the esophagus in this position. In the left oblique position, however (Fig. 4), these did appear very plainly. Conclusion: right-sided aorta.

Case 2. (Borrowed from Harlem Hospital with the kind permission of Dr. William Snow, radiologist.) R. B., colored male, aged 38, admitted to Harlem Hospital Oct. 31, 1932, died Dec. 16, 1932. Diagnosis: essential hypertension, chronic uremia. History: None referable to the anomaly. Physical examination showed the heart to be enlarged to the left. Sounds were of good quality. At the aortic orifice there were soft blowing systolic and harsh diastolic murmurs: over the mitral area, a soft systolic murmur and a snapping second sound (P_2 greater than A_2).

Radiographic examination of the heart (Fig. 5) showed a concentric hypertrophy of the left ventricle. The aortic knob was seen on the right side instead of on the left and the descending aorta was seen to run to the right of the dorsal vertebræ as far as the tenth, where it turned to the left. In the right oblique position (Fig. 6) the aortic knob and the aortic depression in the esophagus were absent but they were plainly visible in the left oblique position (Fig. 7). Conclusion: right-sided aorta.

SUMMARY

1. Right-sided aorta is very rare. It is due to abnormal development.
2. It may occur in pure form or associated with other congenital anomalies.
3. It may not produce symptoms and may be an accidental finding.
4. The roentgen findings are a mirror image of the normal.
5. Two cases are presented, one pure and one with associated interventricular septum defect.

1940 Grand Concourse

THE ROENTGENOLOGIC DIAGNOSIS OF GENERALIZED FETAL EDEMA

By IRA H. LOCKWOOD, M.D., *and* FRED Y. KUHLMAN, M.D., *Kansas City, Mo.*

Generalized fetal edema has been described by Ballantyne (1) as "a morbid condition of the fetus, characterized by general anasarca, the presence of effusions in the peritoneal, pleural, and pericardial sacs, and usually an edema of the placenta, resulting in death of the fetus or infant, before, during, or very soon after birth." The condition has long been recognized, having been described by Guillemeau in 1621. Its incidence has been variously estimated at from 1 in 1,200 to 1 in 3,000 births.

The etiology of generalized fetal edema is obscure. Two general groups of causative factors are noted: (1) abnormality of the fetus itself, and (2) toxic or metabolic derangement of the mother. Broekhuizen (2) classifies the causes as follows:

(*A*) Fetal causes:
1. Heart and vessels:
   (*a*) Fetal endocarditis.
   (*b*) Congenital absence of a chamber of the heart.
   (*c*) Small foramen ovale.
   (*d*) Obliteration of Botallo's duct.
   (*e*) Displacement of heart and vessels due to diaphragmatic hernia.
   (*f*) Situs inversus.
2. Kidneys and genito-urinary system:
   (*a*) Congenital
      (1) Aberrant artery pressing on umbilical veins.
      (2) Cystic degeneration.

Fig. 1. Lateral roentgenogram of abdomen showing wide zone of subcutaneous edema of fetus, particularly of the thighs.

Fig. 2. Postmortem roentgenogram showing edematous condition.

(*b*) Hyperplasia of kidneys.
(*c*) Hypertrophy of kidneys.
(*d*) Fetal nephritis.

3. Liver:
   (*a*) Hypertrophy.
   (*b*) Atrophy and cirrhosis.
   (*c*) Hypertrophy of liver and spleen.
4. Blood:
   (*a*) Fetal leukemia.
5. Fetal syphilis.
6. Fetal peritonitis.
7. Absence of thoracic duct.

(*B*) Due to conditions outside the fetus:
1. Thrombosis of umbilical vein.
2. Edema and hypertrophy of placenta.
3. Hydrops of the entire ovum.

(*C*) Due to remote maternal conditions:
1. Malaria.
2. Endometritis.
3. Hydremia.
4. Leukemia.
5. Chronic nephritis and kidney of pregnancy.

This author does not mention erythroblastosis of the newborn, which seems to be one of the more common causes of universal edema (3).

The importance of prenatal diagnosis of this condition cannot be underestimated, for these infants may be so edematous that a normal delivery is impossible (4). Diagnosis by palpation is usually unsuccessful since hydramnios is frequently present. Insofar as we have been able to ascertain, the roentgenologic diagnosis has not been reported. Gill and Auld (5) mention such a possibility, stating in their report, "a roentgenogram showed a baby of apparent full-term size with flaring ribs and distended arms which, upon delivery, was explained by the edematous condition of the fetal body."

CASE REPORT

Mrs. I. P., aged 26 years, was admitted to St. Luke's Hospital on the service of Dr. Ralph R. Wilson, with a diagnosis of pregnancy (34 weeks), hydramnios, and diabetes mellitus.

Past History.—Third pregnancy. First, five years ago, at which time a very large child died suddenly of an undetermined cause during delivery. Second, three years ago, at which time the diabetes was discovered. Normal baby delivered at term. Since that time the mother has been taking from 30 to 40 units of insulin daily.

Present Illness.—Considerable nausea, with little vomiting early in pregnancy. Last four weeks abdomen has been enlarging rapidly. Three weeks before delivery feet and legs were quite edematous.

Physical Examination.—Enlarged abdomen; McDonald measurement of 43 centimeters. Fetal heart tones were indistinct. Position of

fetus was not well defined. Legs and feet were edematous. B.P. 140/86.

Laboratory Findings.—Urine, positive for sugar with one drop; trace of acetone. Blood Wassermann and Kline negative. Blood counts normal. Blood chemistry: N.P.N. 30; creatinine, 1.6; chlorides, 500; sugar, 282.

Course.—The patient was observed for several days, during which time the diabetes was brought under control. It was decided to induce labor, and an x-ray consultation was requested to exclude a possible hydrocephalus or other type of monster.

X-ray Findings.—"Hydramnios. Normal bony development of fetus. In the lateral projection there is an unusual delineation of the soft tissues of the fetus, with a zone of lessened density in the subcutaneous tissues, varying in width up to one-half inch. This zone contrasts markedly with the denser amniotic fluid and muscle tissue of the fetus. It suggests either an edematous or excessively fat fetus. In view of the fact that the fetus is premature, the latter possibility can be excluded."

Labor was induced and a living child delivered by low forceps. A large amount of amniotic fluid was present which showed a sugar content of 74 mg. per 100 cubic centimeters. There was a large amount of vernix caseosa. The fetus was edematous and purplish in color. Urine obtained five minutes after birth showed a reduction of Benedict's solution with 20 drops, with a trace of acetone and diacetic acid. The child's respiration became labored, the temperature rose to 108.8 F., and death ensued six hours after delivery. A postmortem x-ray negative shows the wide zone of subcutaneous edema.

Summary of Autopsy Findings.—Weight, $9^1/_2$ pounds. Premature. Generalized edema of all tissues; eyes swollen shut; marked swelling of checks and scrotum. Skin purplish in color. Free fluid in pleural, peritoneal, and pericardial cavities. *Liver:* Omental fat and retroperitoneal tissues edematous. *Spleen and testicles:* Congested. *Lungs:* Innumerable small subpleural hemorrhages; massive consolidation, with small areas of crepitation; microscopically the alveoli were filled with a semigranular precipitate, with a pigment which was apparently meconium. *Thymus:* Hyperemia, with small punctate hemorrhages. *Heart:* Subepicardial hemorrhage 1.5 cm. in diameter; separation of muscle fibers by edema; hemorrhage and congestion of myocardium; foramen ovale and ductus Botalli patent, with functioning valve over former. *Pancreas:* Interstitial hemorrhages, with a few lymphocytic foci. *Adrenals:* Extensive hemorrhage with degenerative changes. *Kidneys:* Extensive medullary hyperemia. *Head:* Marked edema of scalp, with hyperemia; tremendous accumulation of subarachnoid fluid flattening the convolutions of the brain; fluid contained 48 mg. sugar per 100 c.c.; falx cerebri and tentorium normal except for hyperemia. Direct blood smears showed no increase in nucleated reds; definite increase in polychromasia. The placenta showed a few scattered infarcts.

Pathologic Diagnosis.—Hydrops fetus universalis; amniotic aspiration pneumonia, bilateral, massive, with punctate hemorrhages of epicardium and pleura; marked subarachnoid edema; slight interstitial pancreatitis.

The postpartum recovery of the mother was uneventful.

Comment.—With improved technic for making short x-ray exposures, we have found it possible, in the lateral projection, to obtain a more or less well-defined outline of the soft tissues of the fetus in a large percentage of the cases in the last two or three months of gestation, without the use of any contrast medium. This definition is apparently caused by the subcutaneous fat of the fetus, contrasting with the denser amniotic fluid and fetal muscle tissue.

CONCLUSION

A case of generalized fetal edema, with hydramnios, due apparently to maternal diabetes, is presented with roentgenologic and pathologic findings. The value of the lateral roentgenogram made with a short exposure time to visualize soft tissues is stressed.

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EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

THE AMERICAN SOCIETY OF X-RAY TECHNICIANS

The tenth annual meeting of the American Society of X-ray Technicians was held in Dallas, Texas, May 21–24, 1935. Several hundred x-ray technicians from every part of the United States were in attendance, representing some of the best known medical schools and hospitals of the country.

The officers who presided at this meeting were: Thomas W. Lough, M.A. R.T., of Seattle, Washington, *President;* Myrtle L. Jones, R.T., of Chicago, *First Vice-president;* Bertha A. Malakowsky, R.T., of Sheridan, Wyoming, *Second Vice-president;* Sister M. Blanche, R.T., of Duluth, Minn., *Third Vice-president,* and Alfred B. Greene, B.Sc., R.T., of Oak Terrace, Minn., *Executive Secretary-Treasurer* and Editor of the journal "The X-ray Technician."

The program consisted of numerous interesting and instructive papers, most of which were on technical subjects of use to those making roentgenograms of the human body. Some of the papers presented described new and most useful technical procedures, which should prove of distinct advantage to many roentgenologists who have to do their own technical work.

The Scientific Exhibit, which presented numerous x-ray film demonstrations of the highest order, was well worth seeing, as it showed the marked progress which is being made in the technical field of roentgenology. This, of course, is very important as every roentgenologist is desirous of producing the very best x-ray films for correct interpretation, and any individual or group of individuals that can make this possible is certainly to be encouraged.

A few years ago, when the American Society of Radiographers, now the American Society of X-ray Technicians, was organized, it met with strong opposition by members of the radiological profession, because at that time, it was thought that members of a technicians' organization would in their enthusiasm carry beyond their limitation and invade the domain of medicine. It is certainly most gratifying to be able to say that time has shown that this organization has kept up the high standards it first set for its membership, and has restricted its activities strictly to the technical field of radiology. Yet, there are some members of the radiological profession who do not yet understand the reason why technicians should be organized, and also what good can come of such an organization. In order to find out first-handed just what the American Society of X-ray Technicians stood for, and what type of membership composed it, and, in fact, to obtain all information possible, your Editor accepted an invitation from this body to be guest speaker at this convention.

I was in attendance from the opening day, until the last day of their meeting. I wish it to be clearly understood that my acceptance of their invitation was not for the purposes just mentioned; as an independent individual, I had long ago formed my own personal opinion of the good they were doing. In accepting their invitation, I felt highly honored, and attended not as a representative of Organized Radiology but as a private in the rear rank. However, as mentioned, it afforded me the opportunity of gathering information which I believed would help to clear away certain misunderstandings in regard to activities which existed in certain quarters.

I was very much impressed by the high degree of intelligence displayed by the members of this organization. Some of them are university graduates, whose academic education would permit them to enter medical school, law school, or a school of engineering; yet, they are content and happy in their chosen field, using their talents in devising better and more practical technical procedures which are proving helpful to radiologists.

One of the interesting observations I made was that at no time did I hear anyone speak of interpretation of x-ray films. I was impressed with their earnestness to comply with their creed, namely, "The Radiographer's Creed." It may be of interest to quote it here.

"We believe that every radiological techni-

cian should work under the direct supervision of, and be directly responsible to, some member of the radiological, medical, surgical, or dental profession, such member being generally recognized in his profession as qualified to do the work attempted.[1]

"We are opposed to the so-called schools (whether conducted by professional men or laymen) that urge the attendance of any or all laymen, with the promise of speedy preparation and handsome remuneration for their services. In other words, we are opposed to the commercial school.

"We believe that the standard for all plate and film work should be established by the professional man doing the work of interpretation, and that it is our duty to qualify ourselves to produce the desired standard."

These lofty ideals are being religiously carried out by the members of this organization. Of course, there is no doubt but that at times some may stray away from the righteous path, but they are promptly dealt with by expulsion. It is obviously true that it is far better for a group of x-ray technicians to be organized, especially so when they have such lofty ideals and can be disciplined when the occasion arises, than to have no such organization, each individual doing whatever pleases him, without restraint.

The subject of the x-ray technician has assumed the proportion of a tremendously important problem for the radiologists to consider. We feel that if the radiologists will make a sincere effort toward a better understanding of what the American Society of X-ray Technicians are doing, and what they stand for, less misunderstanding will occur and a more harmonious relationship will exist between them and the radiologists. I, for one, would be among the first to help suppress any enthusiastic feeling they may have regarding the violation of any medical practice act, but I have no such fear, as I have been sincerely impressed with their honest attitude, restricting themselves purely to the technical phase of radiology. It should be recalled that they have shown quite definitely in the past their desire of co-operating with us. We can all remember that the name under which they first organized was the American Society of Radiographers, which caused dissension among the radiological profession, because it was felt that the word "radiographer" could easily be confused with that of "roentgenography," etc. When their attention was called to this, they submitted the question to some of our most prominent radiologists, who agreed that the word "radiographer" could cause confusion, and, because of this, they voluntarily changed the name to that of "x-ray technician."

The American Registry of Radiological Technicians has several prominent members of the radiological profession who were appointed by our national radiological societies to certify to the qualification of x-ray technicians by examination. Because of this recognition, and because of their adherence to a strict code of ethics, we should give them the encouragement they so well deserve, by helping them increase their membership and by encouraging our own technicians to become registered by examination.

[1] *Editor's note:* Notice that chiropractors, osteopaths, and represenatives of other systems of practice are not mentioned, and I have been assured that they will not enroll as a member any technician who works for such.

SHALL WE TELL CANCER PATIENTS THE TRUTH?[1]

By WRIGHT CLARKSON, M.D., *and* ALLEN BARKER, M.D., *Petersburg, Virginia*

During the past few months several editorials have appeared on this subject. Some authors are opposed to mentioning the word "cancer" to patients, while others feel that they should be told everything. Here, as elsewhere in life, no one rule will apply to every case. If we are dealing with a minor, at least one of the parents should know about the condition. If the patient is mentally deficient, no good will be accomplished by telling him. But in most cases, in which we are dealing with an adult of normal mentality, this question cannot be justly decided by either physician or relative, and, therefore, as often as it is practicable the decision should be made by the patient himself. Those who do not desire to know the truth about their physical condition will often so inform the attending physician, and there is no good reason why the physician should not follow these instructions so long as a lack of knowledge on the part of the patient as to the seriousness of the condition does not interfere with treatment. The physician's sacred duty is to his patient and not to some friend or relative of the patient.

[1] This article has appeared in the June, 1935, issue of Southern Medicine and Surgery.

A physician should not shock a patient by bluntly telling him that he has an incurable cancer. He can always win the confidence of his patient at the first visit by being perfectly honest and saying, "I do not know." This applies equally to the specialist and to the referring physician. The diagnosis in these cases should be made only by those physicians who are specially trained in this field, and should be as accurate as human endeavor can make it. To do this the tissue must be examined under the microscope, and, since proper preliminary irradiation tends to minimize the danger of removing the tissue for examination, the physician has an opportunity during the interval between irradiation and biopsy to convince his patient of the fact that *cancer is curable.* Cancer, in reality, is just as curable as diphtheria, but a patient who receives early treatment for diphtheria and recovers tells his neighbors all about it, while a patient cured of cancer usually prefers not to mention it. Your patient will be interested in learning about this and the fact that a large percentage of the cancers occurring to-day are being permanently cured.

In handling a patient with an apparently hopeless neoplasm, a physician must carefully study the mental as well as the physical aspects of his patient. If, after a careful analysis of a case, the physician is convinced that it is best for the patient not to know the exact status of his condition at that time, he is perfectly justified in withholding the truth temporarily, provided the patient is kept under constant observation and some intelligent and dependable member of the family is informed as to the true condition. For instance, we recently had a patient twenty-seven years of age with a teratoma of the testicle and numerous metastases in his lungs, as shown on roentgenograms. The metastases could not be removed and they proved to be radioresistant. From the rate of growth, we felt certain that the patient could live only about one year, which proved correct, but at the time he was in good physical condition, and he was able to continue his duties for about nine months, in peace, happiness, and without pain. No good could have been accomplished by explaining the true condition to this young man when he first came to us.

A physician should never tell a patient nor his family that his case is hopeless and that he will soon die. We must remember that physicians do not keep the "book of life" and, therefore, such an unqualified statement may prove to be incorrect. In 1930, Dr. J. M. Williams, of Petersburg, Virginia, sent us a patient with a carcinoma of the left breast with metastases in the bones of her hand, pelvis, femur, and one toe. This was proven by microscopic sections examined by many eminent pathologists. We did not expect her to live six months but, following roentgen therapy alone, she is clinically well to-day, five years later, and roentgenograms show no evidence of cancer remaining in her body.

Such cases are rare, but every physician treating a large number of cancer patients encounters frequent surprises at the results obtained in his cases.

Be optimistic to the end, and be honest with your patients. If they really are sincere and persistent in their desire to know the truth, we can see no justification in continuing to deceive them. The fear that accompanies the uncertainty as to the possibility of impending death must be worse than death itself, and while suicides are rare among cancer patients, the few that do occur are usually among incurable cases.

"Honesty is the best policy" here as elsewhere in life, and while in some cases it may be wise to withhold the facts temporarily, it is best to tell the patient the truth in due time, and to request him not to tell those who will constantly remind him of his condition, for it is obvious that curious and inquiring neighbors may create a mental complex that will be detrimental to his physical and social welfare.

ANNOUNCEMENTS

NEXT ANNUAL MEETING

PROGRAM PLANS

During the week that the American Board of Radiology conducted examinations in San Francisco, Dr. Lloyd Bryan, *President,* called an informal meeting of the Program Committee, six members being present, including Dr. Edwin C. Ernst, Chairman of the Publication Committee, and Dr. Leon J. Menville, Editor of the Journal.

The program of the Annual Meeting and the publication of the Journal were discussed, and the President stated that satisfactory progress has been made toward plans for the Annual Meeting in Detroit, next December.

The program will be conducted almost entirely along the symposium line, and the following symposium leaders have been signed up and are now arranging their groups:

Radiation Therapy, Francis Carter Wood, M.D., New York City

Urology, Bernard H. Nichols, M.D., Cleveland, Ohio

Radiation Therapy of Breast Tumors, Albert Soiland, M.D., Los Angeles, California

Bone Pathology, C. G. Sutherland, M.D., Rochester, Minnesota

Co-relation of Physics and Clinical Data of Super-voltage Therapy, R. R. Newell, M.D., San Francisco, California

Thoracic Pathology, Harlan P. Mills, M.D., Phoenix, Arizona

Glands of Internal Secretion, W. H. McGuffin, M.D., Calgary, Canada

Gastro-intestinal Pathology, Leo G. Rigler, M.D., Minneapolis, Minnesota

Radiation of Non-malignant Conditions, Edwin C. Ernst, M.D., St. Louis, Missouri

Symposium on miscellaneous subjects.

The clinics will be in charge of B. H. Orndoff, M.D., of Chicago, and C. K. Hasley, M.D., of Detroit.

Several prominent guest speakers have been arranged with, among them Dr. Chevalier Jackson and Dr. Charles Geschickter, and at least one or two prominent European radiologists.

The Carman Memorial Lecture will be delivered by Dr. Arthur C. Christie, of Washington, D. C.

The scientific exhibits will be in charge of Dr. Paul Titterington, of 212 Metropolitan Building, St. Louis, Mo., and exhibitors are requested to apply directly to him.

MIDSUMMER RADIOLOGICAL CONFERENCE

Denver has a Radiological Club, which will sponsor a Midsummer Radiological Conference, to be held in Denver, Colorado, Thursday and Friday, August 29 and 30, 1935.

The program is as yet tentative, but will probably consist of symposia on Diseases of the Chest, Diseases of the Gastro-intestinal Tract, and Neoplastic Diseases. In addition, it is planned to devote an afternoon to the consideration of the Development, Anomalies, and Diseases of the Spine.

Parts of this program will be given by Denver men, but it is anticipated that several radiologists of recognized standing from other states beside Colorado will present a major part of the program.

In the next issue of RADIOLOGY the Editor hopes to be able to publish the program in full. Meanwhile, inquiries may be addressed to Frank B. Stephenson, M.D., Metropolitan Building, Denver.

LATIN-AMERICAN CONGRESS OF PHYSICAL THERAPY, X-RAY, AND RADIUM

The Latin-American Congress of Physical Therapy, X-ray, and Radium will hold its first annual meeting in Mexico City from August 29 to September 5, it is announced by Dr. Cassius Lopez de Victoria, Executive Director of the organization. The National University of Mexico will act as host to their North American colleagues, and the Government will participate in extending hospitality to the delegates.

To facilitate the attendance of American physicians at this Congress, a nineteen-day convention cruise has been arranged, with steamer, rail, hotel, and sightseeing costs included in one all-expense fee. The convention cruise and all of its advantages will be available not only to the physicians, but to members of their families and their friends.

Five special tours to the Latin-American Congress and return have been arranged by the American Express Company, that has been asked to direct the Congress Cruise. The first of these, which is expected to prove most popular is a round-trip by steamer, the S. S. *Yucatan* having been especially chartered for the purpose of the Congress.

It will also be possible for physicians to make the round-trip by rail, or to go by steamer and return by rail. Special arrangements have also been made for a return trip by rail, including a stop-over at Kansas City, for those who desire to attend the Fourteenth Annual Scientific Session, Congress of Physical Therapy, on September 9, 10, 11, and 12.

In addition to first-class hotel accommodations in Mexico City, delegates registered for the cruise will enjoy sightseeing trips to principal points of interest in Mexico City, a thirty-mile drive to the pyramids of Buried City of San Juan Teatihuacan, all-day water trips to Xochimilco and the Floating Gardens, to Cuernavaca, to Toluca, and to the Desert of the Lions. On the outward-bound trips the

cruise will stop at Havana, and Progreso, and returning will call again at Havana.

The medical activities of the Congress will be held in the faculty rooms of the National University School of Medicine and will be divided into sections representing medicine and surgery, fractures in their various specialties, electrosurgery, fever therapy, short and ultra-short wave therapy, light therapy, massage, radium, x-ray therapy, and exercise.

The officers of the Congress are Norman Edwin Titus, M.D., *President;* William Bierman, M.D., *First Vice-president;* Heinrich Franz Wolf, M.D., *Second Vice-president;* Madge C. L. McGuiness, M.D., *Secretary,* and Cassius Lopez de Victoria, M.D., *Executive Director.*

Delegates to the Congress desiring to present papers will submit the titles of their papers, together with an abstract, to either Dr. Madge C. L. McGuiness, 1211 Madison Avenue, New York City, or Dr. Cassius Lopez de Victoria, 1013 Lexington Avenue, New York City.

COMMUNICATIONS

FLORIDA STATE RADIOLOGICAL SOCIETY

The regular annual meeting of the Florida State Radiological Society was held May 12, 1935, at the Harrington Hall Hotel, Ocala, Florida.

This meeting was held in conjunction with that of the Florida State Medical Society. The usual round-table discussion of interesting and puzzling cases, which has been the method adopted by the Society since its inception, again proved eminently satisfactory. There were numerous visitors from the general session who made favorable comments on the character of the meeting.

The following officers were elected for the ensuing year: W. McL. Shaw, M.D., of Jacksonville, *President;* F. J. Payton, M.D., of Miami Beach, *Vice-president;* Gerard Raap, M.D., of Miami, *Secretary-Treasurer.*

The next annual meeting will be held in May, 1936, in Miami. The place of the semi-annual meeting is yet to be determined.

TULANE UNIVERSITY SCHOOL OF MEDICINE CELEBRATES ITS ONE HUNDREDTH ANNIVERSARY

The following communication is an abridgement of a news release received from the Secretary-Treasurer of the Society. The Editor of the Journal, being head of the Department of Radiology, of Tulane University School of Medicine, was reluctant to write about the event, but, upon receiving this material from Dr. Donald S. Childs, he concluded that the whole country might have a certain interest in what is a matter of deep significance to the South. It is to the Editor a matter of profound satisfaction that the youngest specialty, radiology, was so honored that they chose him to act as Ivy Day Orator. Radiology is giving a good account of itself here in the South, as witness the courses of instruction offered in the leading medical schools.

The sketch of the Tulane University School of Medicine celebration follows:

"In commemoration of its achievement of a full century of medical and other higher education, Tulane University of Louisiana celebrated (June 8–12, 1935) with an elaborate program, including the awarding of honorary degrees to thirteen outstanding Americans; course degrees to approximately five hundred men and women, and special exercises by the various colleges and their alumni. . . . A number of prominent speakers took part. Not only will credit be given to the Tulane School of Medicine for its notable contributions to medical research and clinical application and practice, but also for its large contribution to the health and well-being of the people of the South, Southwest, and Central America, through the 6,500 and more doctors which Tulane has graduated during the century of its existence.

"Located adjoining the great, State-operated Charity Hospital, in the port city of New Orleans, equipped with the most modern and expertly planned medical plant in the South, with a faculty of more than 150 recognized medical experts, and with unexcelled facilities for practical, clinical teaching, the Tulane School of Medicine, and the Graduate School of Medicine to-day present a vivid contrast with the beginning one hundred years ago. The genesis and history of what is now the Tulane School of Medicine is most colorful. In 1833, New Orleans, then a city of only 50,000 inhabitants—with a scarcity of doctors, and no facilities for medical education—was visited by such a scourge of cholera and yellow fever that 6,000 of its people died. The seriousness of the need and the opportunity afforded by Charity Hospital for research and clinical teaching were recognized by three young physicians, Dr.

Thomas Hunt, of South Carolina, Dr. Warren Stone, of Vermont, and Dr. John M. Harrison, of Washington, D. C., who had migrated to New Orleans during this epidemic. Through the energy, initiative, and persistent effort of these three immortal young men, the Medical College of Louisiana was established in the latter part of the year 1834.

"Twelve years later, in 1847, this Medical College was incorporated as the Medical Department of the University of Louisiana, which, through a grant by the State Legislature, was established in New Orleans, with the departments of Medicine, Law, and Arts and Sciences. In 1884, Paul Tulane, a resident of Princeton, N. J., who had amassed a large fortune as a merchant in New Orleans before the Civil War, and who appreciated the lack of an adequate university educational system in the South, made what was in those days a princely gift of more than a million dollars to endow an institution for the higher education of the white youth of New Orleans and Louisiana. Through direct purchase, the University of Louisiana became the nucleus of the present Tulane University of Louisiana. In addition to the original three schools—Schools of Medicine, Law, Arts and Sciences—the University now includes: the Graduate School; the Graduate School of Medicine; the College of Engineering; the H. Sophie Newcomb Memorial College for Women; the College of Commerce and Business Administration; the School of Social Work; the Department of Middle American Research, and the Summer School.

"Pioneering and leading in the study of tropical diseases, the members of the Tulane Medical Faculty and alumni have made important contributions to the knowledge and control of diseases peculiar to tropical climates, such as malaria, yellow fever, cholera, beri beri, leprosy, amoebic dysentery, etc. Its graduates have achieved distinction in all branches of medicine. To mention only one—Dr. Rudolph Matas, now Professor Emeritus of Surgery for his *alma mater*, has gained international renown for his contributions to the science and practice of vascular surgery. Dr. Matas holds a long array of titles and honors from medical schools and medical associations throughout the world.

"The fact that New Orleans is to-day a healthy city of a half-million population, and is recognized as one of the world's outstanding medical centers, is due in great measure to the hundred years of effort of the School of Medicine of Tulane University. From every State, and from almost every country of the world, men and women have come to Tulane for a medical education. . . ."

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ACTINOMYCOSIS

The Roentgen Treatment of Actinomycosis of the Internal Organs with the Protracted Fractionated Method. K. Breitländer. Röntgenpraxis, January, 1935, **7**, 35, 36.

The results in the Clinic at Zürich, in actinomycosis of the jaw have proved that the protracted fractionated method of irradiation marks progress in the treatment. A case of an extensive actinomycosis of the anterior half of the bladder and of the mesentery, proved by operation, biopsy, and microscopic examination, is reported. Treatment consisted of 1,560 r, given over the bladder region in 13 treatments (180 K.V., 2 mm. Cu). The patient recovered and has remained symptom-free for two years.

HANS W. HEFKE, M.D.

APPARATUS

On the Therapeutic Importance of the Secondary β-rays. Sven Benner and Björn Snellman. Acta Radiologica, 1935, **16**, 233–241.

The secondary β-radiation from platinum filters has greater biologic effect than that from palladium filters. The experimental results make it dubious whether the new Pd needles offer an advantage in treating the skin and mucous membranes. The difference in the treatment of interstitial tissues with the two types of filters could not be detected.

G. E. BURCH, JR., M.D.

A Direction Indicator for Roentgen Tubes. Magnus Strandqvist. Acta Radiologica, 1935, **16**, 304–309.

An apparatus is described for directing roentgen tubes in the treatment of deep-seated tumors through small portals. The apparatus is simple and easily manipulated. From the horizontal and vertical distance between the center of the tumor and the "centering point" in the field, the tube is accurately adjusted. This adjustment can be easily reproduced at each succeeding treatment.

The author concludes: "In diagnostic examinations the instrument can also be used to work out standard adjustments and accurate duplications of these."

G. E. BURCH, JR., M.D.

BIOLOGIC EFFECTS

Comparison of the Effect of Roentgen Rays on Mutations in the Fruit Fly. Artur Pickhan. Strahlentherapie, 1935, **52**, 369–388.

Extensive studies of the effect of roentgen rays and radium on mutations in the fruit fly show that there is a linear relation between dose and rate of mutation. Experiments carried out to determine the influence of the time factor revealed that the formula $K = I \times t$ holds for both roentgen rays and radium. In contrast to some American investigators, the author found that equivalent doses of roentgen rays and radium produce the same effects on mutations.

ERNST A. POHLE, M.D., Ph.D.

Irradiation of Chicken Embryo *in vitro* and *in vivo* with Gamma Rays of Radium. C. W. Wilson, A. F. Hughes, A. Glücksmann, and F. G. Spear. Strahlentherapie, 1935, **52**, 519–524.

This paper was presented before the Fourth International Congress on Radiology in Zurich and can be found in English in the proceedings of the Congress.

ERNST A. POHLE, M.D., Ph.D.

BLOOD PRESSURE

The Effect of Irradiation on Blood Pressure. S. Belák and A. Uhrovits. Strahlentherapie, 1935, **52**, 692–698.

Following an exposure to ultra-violet rays (quartz mercury vapor lamp) the blood pressure drops first and then increases. Exposures of 20 seconds have a definite effect. If the exposure is repeated, it is always followed by an increase in blood pressure provided that the reaction of the first exposure has subsided. Heat radiation has no definite effect. If ultra-violet rays and heat are combined, only a lowering of the blood pressure is observed; it seems as if the heat radiation suppresses the secondary increase of blood pressure observed after ultra-violet exposure alone.

ERNST A. POHLE, M.D., Ph.D.

BONE DISEASES (DIAGNOSIS)

A Contribution to the Factor of Heredity in Marble Bone Disease. Alexander Pagenstecher. Röntgenpraxis, January, 1935, **7**, 14–16.

The literature of the marble disease of bones is reviewed, especially in reference to heredity. The author reports this disease in a 65-year-old farmer and his 25-year-old son. In both cases the finding was accidental.

HANS W. HEFKE, M.D.

CANCER (DIAGNOSIS)

Early Diagnosis of Gastric Cancer. F. Schreiber-Ermer. Wien. med. Wchnschr., Nov. 17, 1934, **84**, 1269. (Reprinted by permission from British Med. Jour., March 2, 1935, p. 35 of Epitome of Current Medical Literature.)

The author records several cases of carcinoma of the stomach responding satisfactorily to resection, thanks to the early diagnosis, which depended on the attention paid to apparently minor symptoms. In one case the first symptom was pain felt on bending; there was no pain on eating, the appetite was good, and there was apparently no other symptom to incriminate the stomach. Had the pain on bending been ignored, the x-ray examination and subsequent operation would doubtless have been deferred till the case was inoperable. In another case the only symptoms were loss of appetite, giddiness, lassitude, and some loss of weight. After being treated for arteriosclerosis for four months by another practitioner the patient came to the author, who was struck by the grayish-yellow tint of his skin. It was this tint which led to an x-ray examination and successful operation for cancer of the stomach. In a third

case—that of an elderly woman—the only symptom was slight pain in the region of the left costal arch when she turned onto her left side in bed. Otherwise she felt in the ruddiest of health, and she looked perfectly well. In yet another case the only symptoms were loss of appetite and flatulence. The moral of these and several other cases is that early malignant disease of the stomach may be diagnosed by the help of the x-ray if the practitioner pays attention to seemingly trivial warnings.

CANCER (THERAPY)

The Problem of Radiation Therapy in Carcinoma of the Esophagus. Karl Wasserburger. Strahlentherapie, 1935, **52**, 611–616.

The author studied the efficacy of radium therapy in carcinoma of the esophagus. Three to four screens containing 13.2 mg. ra. were placed in a soft stomach tube so that a total of from 40 to 53 mg. ra. were distributed over from 66 to 88 millimeters. The dose amounted to from 21 to 28 mc. during a period of from 70 to 80 hours with daily exposures of from 4 to 6 hours. The filter was 1.5 mm. Pt plus 2 mm. Al; the distance between radium screen and mucous membrane corresponded to approximately from 5 to 8 millimeters. Eleven out of the 27 patients admitted were treated. Some obtained temporary relief even up to the point of being able to swallow solid food. It is advisable to insert the stomach tube first without radium screens in order to test the reaction of the patient. If the manipulation is followed by a rise in temperature, it is inadvisable to start treatment. Metastatic glands require roentgen therapy. A number of roentgenograms showing the findings before and after treatment are appended.

ERNST A. POHLE, M.D., Ph.D.

Fractional or Single Massive Dose Method in the Treatment of Cancer. A. Frank. Strahlentherapie, 1935, **52**, 602–610.

The author irradiated with roentgen rays an epithelioma of the skin 10 cm. long, 8 cm. wide, and 1 cm. thick located in the right upper quadrant. One-half of the tumor received 20 daily treatments of 200 r each while the other half received 1,800 r in one single dose. After the application of 1,000 r in fractional doses there was definite regression macroscopically, while the half treated with the single massive dose did not show any changes. This difference in reaction was more marked after the fractional dose side had received a total of 1,800 r. Biopsies were taken of both halves of the tumor on the twelfth day and photomicrograms showing the histologic findings are appended to the paper. There are also photographs of the tumor at various intervals. On the eighty-first day following the first treatment there was still a residual tumor mass on the part which had received the single massive dose, while the other half had healed. By adding 2,150 r in daily doses of from 200 to 250 r, complete healing was brought about. It is concluded, therefore, that the fractional dose method is preferable in the treatment of carcinoma because the tumor disappears completely with less injury to the surrounding skin and regression begins at an earlier date than with the single massive dose method.

ERNST A. POHLE, M.D., Ph.D.

FOREIGN BODIES

Bullets in the Lung Tissue and Their Sequences. K. Ulrich. Röntgenpraxis, March, 1935, **7**, 145–156.

Bullets were found embedded in the lung tissue without formation of a fibrous tissue capsule around them. It is very improbable that bullets may change their position in the lungs. Adhesive pleurisy, quite often with calcification, is a common sequence, especially after a hemato-thorax. When cavities are formed in the lung tissue, the bullets may be freely movable in them. Tuberculosis may be found independent of the injury, but may also be caused by it.

HANS W. HEFKE, M.D.

The Functional Findings and the Roentgen Diagnosis in Foreign Bodies in the Heart. M. I. Glikin. Röntgenpraxis, March, 1935, **7**, 185–187.

Foreign bodies in the heart are rare and their roentgenographic localization is of interest. In the case reported, the patient complained of no symptom, but gave a history of a suicidal attempt. Roentgenograms of the chest and fluoroscopic examination showed a bullet in the region of the right ventricle. It moved with the pulsation of the heart, mostly up and down, and the amplitude of pulsation was about one and one-half centimeters. If the mechanics of heart construction are considered, it should be possible to make a correct diagnosis of the situation, of a foreign body in the heart, in most cases.

HANS W. HEFKE, M.D.

GASTRO-INTESTINAL TRACT (DIAGNOSIS)

Chronic Intermittent Duodenal Stasis. Julius Friedenwald and Maurice Feldman. Am. Jour. Roentgenol. and Rad. Ther., August, 1934, **32**, 161–166.

The etiology of this condition may be due to (1) arterio-mesenteric compression of the duodenum, with visceroptosis; (2) movable tumors or masses producing pressure, also spinal deformity, movable growths or pressure from ptosed kidney or calcified glands; (3) adhesions and congenital bands or reflex disturbances of the duodenum from lesions elsewhere in the gastro-intestinal tract; (4) stretching and sagging of the duodenum due to overloading; (5) dysfunction of the neuromuscular mechanism of the duodenum.

The greatest incidence of this condition is in middle life and in females. The symptoms are not always characteristic, especially in the mild form. Frequently, however, periodic bilious attacks occur, with nausea and vomiting, intermittently over many years, often from childhood. Nervous strain tends to induce attacks. The onset is often preceded by constipation and headaches. Diarrhea may alternate with con-

stipation. Change in posture may relieve the pain. Loss of weight and strength, associated with extreme exhaustion as well as mental depression and neurasthenic symptoms, may occur. During an attack, epigastric distress, fullness, eructations of gas, and epigastric pain usually occur. Occasionally pain may extend to the gall-bladder region and the liver may enlarge.

Roentgenologically, duodenal stasis is most satisfactorily demonstrated in the upright posture. In the mild cases, demonstration of the disease may be very difficult. Between attacks, no stasis is seen. A rapidly emptying stomach, by distending the duodenum, may simulate the condition. To eliminate this condition, the duodenum must be examined at intervals over a period of at least 30 minutes. In the marked cases, a 6-hour gastric and duodenal retention may be present. Regurgitation into the duodenal bulb may occur. The bulb may be elongated, dilated, and present a delay in the expulsion of the contrast substance. In most of the cases observed, the stasis occurred in the second portion.

Treatment is medical in most cases. The visceroptosis is treated in the usual fashion and the diet is bland, but so planned as to produce gain in weight. Bed treatment is necessary in severe cases. Surgery is employed as a last resort—either a duodenojejunostomy or a division of constricting bands.

S. M. Atkins, M.D.

Small Intestinal Invagination Caused by a Meckel's Diverticulum. Egon Reiser. Röntgenpraxis, February, 1935, **7,** 90–94.

A Meckel's diverticulum had led to symptoms of small intestinal obstruction in a 34-year-old patient, causing an invagination of about ten inches of the terminal ileum. The roentgenologic diagnosis had been small intestinal obstruction, without showing the correct cause for it. The author believes that small amounts of barium meal, given at short intervals, and oft-repeated roentgenograms should be employed for a more complete diagnosis.

Hans W. Hefke, M.D.

Diverticulosis of the Colon. G. Bignami. Arch. di Radiol., September-October, 1934, **10,** 517–531.

Professor Bignami, of Pavia, points out that it is only by x-ray examination that a definite diagnosis of diverticulosis of the colon can be made, and gives the data on two illustrative cases.

E. T. Leddy, M.D.

The Migratory Cecum. Jacob Buckstein. Am. Jour. Roentgenol. and Rad. Ther., August, 1934, **32,** 171–178.

The mobile cecum is due to an abnormally long mesentery and, in itself, is not pathological, although under certain conditions, particularly as the result of kinking or axis rotation, it may produce symptoms, as follows: (1) intermittent colicky attacks of pain over the cecum or ascending colon, without fever; (2) chronic constipation, occasionally severe, alternating with diarrhea of short duration; (3) a tumor in the cecal region which feels as if it contained fluid and air. Confirmation depends on roentgen examination, demonstrating abnormal mobility of the cecum together with dilatation and stasis within it. Symptoms may also be produced by the full ptosed colon causing traction on the duodenum or gall bladder.

The medical treatment consists of attention to the associated intestinal stasis and ptosis. A cellulose-rich diet is contra-indicated. Cecal fixation is advised by surgeons.

S. M. Atkins, M.D.

GRENZ RAYS

Beneficial Effect of General Body Exposure to Grenz Rays in Severe Pain Due to a Blood Vessel-nerve Tumor. G. Schulte and T. Isselstein. Strahlentherapie, 1935, **52,** 646–651.

The author reports an unusual case presenting numerous small extremely painful tumors of pea to walnut size distributed over various parts of the body. Histologically, they appeared to be a mixture of nervous and blood vessel elements, perhaps belonging to the group of glomus tumors. Exposure to Grenz rays (9 K.V., 10 ma., 10 cm. F.S.D., 750 r every second day) brought considerable relief. A recurrence of the symptoms two years later responded again to the same treatment.

Ernst A. Pohle, M.D., Ph.D.

GYNECOLOGY AND OBSTETRICS

Radium Therapy in Gynecological Bleedings. H. Naujoks and H. Hoffmann. Zentralbl. f. Gynäk., Aug. 18, 1934, **58,** 1922–1935. (Reprinted by permission from British Med. Jour., Dec. 8, 1934, p. 88 of Epitome of Current Medical Literature.)

The authors report that at the Marburg Universitäts-Frauenklinik radium treatment plays an increasing part in the therapy of metrostaxis due to benign disease, and in this connection has almost completely replaced x-radiation. The great majority of cases of "non-malignant bleeding" which are treated by radium are those of women over 40 who have menorrhagia or metrorrhagia in the absence of any important morbid physical findings on bimanual examination: pathologically they fall in the groups of chronic induration, myomatosis, metropathia hemorrhagica, or glandulocystic hyperplasia. Together with 252 cases of this description, radium treatment was given for "benignant bleedings" in 25 cases of myoma (including six of submucous myoma), two of blood disease with severe metrorrhagia, two of severe bleedings of puberty, and two of therapeutic sterilization. At Marburg operative treatment of myoma is the rule, radium therapy being reserved for occasional cases of very small myomas, or as a life-saving measure (because of the very prompt stoppage of the bleeding) in exceptionally blanched patients with large myomas. In bleeding at puberty radium is required—very, very rarely—as an alternative to hysterectomy in critical cases: in both the patients treated by radium the menses returned after a few

months. The application of the radium, within the uterus, in a single dose of 50 mg. applied for twenty-four to forty-eight hours, is preceded immediately by curetting, and is never undertaken unless careful clinical examination has shown signs of inflammation, such as pyrexia, and abnormal erythrocyte sedimentation time to be absent. In seven instances of 285 the histological examination of the curettings showed a carcinoma of the corpus uteri: a second radium application was given a few days later and followed by x-radiation, and cure appeared to be attained in all.

In the very great majority of cases of "non-malignant bleeding" the radium treatment had a prompt and satisfactory result, three-quarters ceasing to bleed after the radiation and nearly a quarter having only one more hemorrhage. One lethal case (from embolus), one abscess in the pouch of Douglas, and one femoral thrombosis were the total morbidity findings after 285 applications of radium. Menopausal symptoms were not severe.

The mode of action of radium in these "non-malignant bleedings" is not clear. While not denying the possibility of ovarian affection, especially with large doses, Naujoks and Hoffmann are inclined, from the results of tests for folliculin and antuitrin in the blood, to look on the treatment as affecting chiefly the uterus, of which the lining is known to become structureless and necrotic without the cavity being obliterated.

Roentgen-ray Dosimetry in the "Third Dimension" in Gynecology. F. Friedl. Strahlentherapie, 1935, **52,** 664–670.

The author discusses the various technics used in gynecologic radiation therapy. For carcinoma of the cervix he recommends one anterior, one posterior, and two lateral fields of 15 × 10 cm., and in some cases a vulva field is added. The dose effective in the tumor is 600 r. Preceding the first roentgen treatment he administers 30 mg. ra. to give a dose of 1,000 mg.-hr. in the cervix, and 60 mg. ra. in the vagina to give there a total dose of 2,000 mg.-hr., filtered through 3 mm. Pb or its equivalent in one sitting. Three weeks after this first radium treatment a second application is given, while roentgen therapy is repeated three months later. Roentgen sterilization is best carried out with one large anterior and posterior field and 300 r effective in the ovaries.

ERNST A. POHLE, M.D., Ph.D.

X-rays in Obstetrics. K. Heyrowsky. Med. Klinik, Dec. 7, 1934, **30,** 1630–1632. (Reprinted by permission from British Med. Jour., March 30, 1935, p. 54 of Epitome of Current Medical Literature.)

The author, in discussing the indications for x-rays in obstetrics, states that they are required only in rare cases when all other diagnostic methods have failed. When x-ray plates are necessary they can be taken without any discomfort to the patient, under strictly aseptic conditions, and without the slightest fear of danger to the fetus. A plate taken in the coronal plane is of relatively little value, except when there is a suspicion of plural births, death of the fetus, and fetal malformations. The author has frequently diagnosed the latter in the presence of hydramnios, especially when indistinct fetal heart sounds could be heard but no movements could be felt. A plate in the sagittal plane is of more value, as in it the relation of the fetal head to the pelvis may be estimated. It is indicated in contracted, funnel-shaped, and rickety flat pelves, in spondylolysis and spondylolisthesis. An axial exposure, which is technically a difficult procedure, gives the best results when the pelvis is obliquely contracted or asymmetrical. For a correct estimation of the degree of flexion lateral and dorso-ventral plates are required. X-rays are valueless in determining the actual measurements of the fetal head.

Editor's Note.—This is not in agreement with opinion in this country.

HAY FEVER

Experience in the Treatment of Hay Fever and Rhinitis Vasomotoria. Lilly Pokorny. Strahlentherapie, 1935, **52,** 656–659.

The author reports six cases of hay fever and rhinitis vasomotoria which were treated by roentgen rays. Technic: 220 r through 0.2 mm. Cu plus 1 mm. Al over the nose in adults; in children the dose is less according to the age; the interval between series, four weeks. Five of the patients were cured.

ERNST A. POHLE, M.D., Ph.D.

HEART AND VASCULAR SYSTEM

The Roentgen Diagnosis of Atherosclerosis of the Thoracic Aorta. A. Baranova. Röntgenpraxis, March, 1935, **7,** 175–182.

Dilatation and tortuosity of the aortic shadow, change in the character of the pulsation, and greater intensity of the aortic shadow have been generally considered diagnostic for therosclerosis of the aorta.

The widening and elongation of the aorta may be caused by different pathologic processes. The changes of old age alone may cause them, as well as a change in the character of pulsation. These roentgenologic symptoms do not allow a differentiation between atherosclerosis and loss of elasticity due to old age.

The third symptom, that of greater intensity of the aortic shadow, has been studied by the author. By making roentgenograms of pieces of different aortas from autopsy material the different stages of atherosclerosis were examined. There was no appreciable difference in the intensity of the shadows. Only when there were calcium deposits, these areas were increased in density, but only in isolated spots. The roentgenologic symptom of a diffuse intensification of the shadow of the aorta is, therefore, unreliable as far as the diagnosis of atherosclerosis is concerned. The finding of calcified areas or plaques is of roentgenologic significance only. The difference in the intensity of the aortic shadow rather is determined by its diameter and factors which influence the intensity of the surrounding areas.

HANS W. HEFKE, M.D.

Aneurysm of the Abdominal Aorta. Werner Hollmann. Röntgenpraxis, December, 1934, **6,** 811–814.

Aneurysms of the abdominal aorta are very difficult to diagnose clinically; roentgenologically, a diagnosis is possible only by effects of the aneurysm on neighboring organs, especially erosion of the spine. The anterior aspects of the twelfth dorsal and first lumbar vertebræ in this case show a halfmoon-like destruction; to the left of the spine there were some areas of calcification. The thoracic aorta showed roentgenologic signs of a syphilitic aortitis. The positive Wassermann reaction and the roentgenologic signs suggested the diagnosis of an aneurysm of the abdominal aorta. Clinically there were angio-spastic pains and neuralgic pains in both legs, which made the patient bedridden. Treatment with iodine and mercury improved the patient so much that he was able to be up and about again.

HANS W. HEFKE, M.D.

A Typical Case of Aneurysm of the Heart. H. Regelsberger. Röntgenpraxis, December, 1934, **6,** 806–811.

Clinically diagnosed and roentgenologically demonstrated, aneurysms of the heart itself are as yet rare in the medical literature. Such a case is reported with autopsy findings. There was a sac-like, fairly well circumscribed bulging at the left border of the heart, which corresponded with the position and size of the aneurysm at the autopsy.

HANS W. HEFKE, M.D.

Cardiospasm or Hiatus-spasm (?). Theodor Bársony and Ernst Koppenstein. Röntgenpraxis, February, 1935, **7,** 73–79.

There is spastic narrowing of the cardia as well as of the hiatus when one speaks of functional cardiospasm. A definite localization of the spasm is possible roentgenologically in the greatest number of cases. The differentiation between the two places of constriction is necessary, especially when surgical intervention seems indicated.

HANS W. HEFKE, M.D.

THE HIP JOINT

Otto's Disease and Other Forms of Protrusio Acetabuli. Kristian Overgaard. Acta Radiologica, 1935, **16,** 390–410.

The term "protrusio acetabuli" has been applied to a number of cases of deformities of the pelvis, the common feature being a protrusion of the acetabulum more or less deeply into the lumen of the small pelvis, associated with a medial displacement of the contents of the hip joint. This condition was first described in 1824 by A. W. Otto, who reported a case of bilateral protrusion of the hip-sockets.

A careful survey of the literature and of his own cases has convinced the author that these cases fall naturally into two large and one smaller third group.

The first group, designated as "secondary protrusions," comprises those cases in which it may be directly inferred from the history or from the specimen that there has been a clearly traceable focal destructive disease in the socket of the diseased hip joint, or a trauma. In these cases, the disease, as a rule, appears only on one side, and the protrusion must be regarded as a direct consequence of the destructive process and the subsequent healing.

The second group includes those cases of true "Otto's disease" and has been called "osteo-arthritic protrusions." In these cases the condition appears without a traceable focal disease, is usually bilateral and limited to the acetabulum itself. It has been regarded as a special form of the deforming osteo-arthritis of the hip joint. A certain form of development of the hip-socket is thought to be a contributive factor, or the chief cause of the development of the disease. The onset of the condition is usually insidious and protracted and frequently the deformity appears as an accidental discovery.

The third and smallest group has been classified as "juvenile osteo-asthenic protrusions." This disease occurs in young women at about the age of puberty. There are no evidences of previous focal disease or trauma of the hip joint. It is believed to result from a lessened resistance of the bone tissue.

The author reports 13 new cases, illustrating the three types of protrusio acetabuli.

J. N. ANÉ, M.D.

INFLAMMATORY DISEASES

Indications of Roentgen Therapy in Non-malignant Ano-rectal Disease. Bensaude, Solomon, and Marchand. Strahlentherapie, 1935, **52,** 660–663.

The authors have observed good results in the treatment of fistula, fissura ani, and thrombosis in hemorrhoids. From 150 to 225 r are given per sitting up to total doses of from 1,400 to 2,000 r. It is advisable to use heavy filtration. In pruritus ani, condyloma, and inflammatory processes of the rectum good results may also be obtained.

ERNST A. POHLE, M.D., Ph.D.

The Experimental Foundations of Roentgen Therapy in Acute Inflammatory Disease. J. P. Mischtschenko, M. M. Fomenko, T. F. Feszenko, S. N. Ledanow, and A. W. Morgatschow. Strahlentherapie, 1935, **52,** 464–496.

It is well known clinically that the roentgen ray has a beneficial effect in many cases of inflammatory disease; however, its mechanism is still unknown. The authors undertook, therefore, a series of clinical, morphological, serobacteriological, chemical, and physicochemical studies in order to shed some light on this problem. They found that the optimal dose in rabbits was 80 per cent H.E.D.; in guinea pigs, 60 per cent H.E.D., and in man from 20 to 30 per cent H.E.D. (the latter corresponds probably to from 120–180 r). During the initial stage of inflammation, higher doses may be required. Studies of the blood and the local cell reaction showed that there is an increase in the decomposition of leukocytes and also in the phagocytosis

following irradiation. In all probability non-specific antibodies are formed. Aminoacids and trypsin are increased following irradiation. No reaction could be found in the small blood vessels as studied on the ear of the rabbit. The analgestic effect of roentgen rays in inflammatory diseases may be due to the influence of decomposed proteins and lipoids on the nerve ends.

ERNST A. POHLE, M.D., Ph.D.

THE KNEE JOINT

Pellegrini-Stieda's Disease (Post-traumatic Calcification of the Collateral Tibial Ligament of the Knee). Max Ritvo and Joseph Resnik. Am. Jour. Roentgenol. and Rad. Ther., August, 1934, **32,** 189–195.

Pellegrini-Stieda's disease is a post-traumatic calcium deposit in the region of the collateral tibial ligament of the knee, and roentgenologically is seen medial to the inner condyle of the femur. The calcification is not visible until two weeks or more after the injury, therefore, repeated roentgen studies are necessary. Pellegrini made the first report in 1905 and Stieda, independently, in 1908.

This condition may be produced by direct or indirect trauma, severe or slight. Microscopically, the calcified mass is definitely bony in character. Directly following the trauma the symptoms are those following injury to the knee, but they fail to subside. In those of months or years' duration there is limitation of motion of the knee joint. A sense of resistance and thickening is present over the inner aspect of the knee. The mass may be palpable and slightly movable. Tenderness is not necessarily present in the late stages.

Roentgenologically the mass is usually a semilunar calcification just medial to the inner condyle of the femur, but the shape and size may vary and enlarges as disease progresses. The older the condition, the denser it becomes. There is never any connection to the femur. This is an important differential point.

Treatment in the acute stage consists of rest and physiotherapy, as in subdeltoid bursitis, and, if this fails, surgery is advised. Reports on 11 of the authors' cases are included.

S. M. ATKINS, M.D.

THE LUNGS

The Situation of the Pleural Exudate in Obstructive Atelectasis of the Lung. Nils Westermark. Acta Radiologica, 1935, **16,** 345–353.

The author reports 13 additional cases of paradoxical situation of free pleural exudate associated with massive collapse of the lung. Jacobæus and the author have previously reported five cases of the same condition in which the occlusion which led to the massive pulmonary collapse was due to bronchial cancer. In the present series of 13 cases, bronchial occlusion resulted from bronchial cancer in six cases; from tuberculosis in four cases; from pleuro-pneumonia and bronchiectasis in two cases, and from trauma in the lung in one case. In the 18 cases observed by the author the free exudate had a sharp upper border which extended obliquely laterally and downward instead of, as usual, obliquely medially and downward.

The situation of the free pleural exudate was found to vary, depending particularly on the site of the obstructive atelectasis and to a certain extent on the amount of exudate and atelectasis and their relation to one another. When the atelectasis was noted in the lower and middle lobes or in the anterior inferior part of the left upper lobe, the exudate was always situated near the atelectasis. With atelectasis of the posterior medial portion of the lower lobe, the exudate lay posteriorly and medially. With atelectatic involvement of the middle lobe or lower part of the left upper lobe, the exudate was found anteriorly and medially. When the shadow of the exudate partially or completely covers the area of obstructive atelectasis, a determination of the position of the exudate enables one to diagnose the site of the atelectasis and thus of the one or more occluded bronchi.

In the author's opinion the situation of the free pleural exudate is determined by the following factors: (1) the weight of the exudate, (2) the compressibility of the surrounding tissues especially of the lungs, (3) the retractivity of the lung, and (4) the pressure conditions within the pleural cavity. It is believed that the lung has its greatest retractivity in the periphery far from the hilus. It, therefore, follows that the basal, lateral, and posterior portions of the lower lobe are the most compressible and have the greatest power of retraction in the normal lung. With the patient in an upright position the exudate in the case of the normal lung is situated inferiorly, laterally, and posteriorly and gives the picture of a massive density which on a frontal view has an upper border running obliquely medially and downward. On the lateral view the exudate is situated mainly posteriorly and has a border which passes obliquely anteriorly and downward. These findings, however, are dependent upon the preservation of the normal elasticity and negative pressure in the pleural cavity. If that elasticity is interfered with for any reason or the negative intrapleural pressure changed, the roentgen appearance of the fluid will take on a different form.

In an obstructive atelectasis in a case in which the medial portions of the lung close to the hilum are collapsed and retracted, the exudate must take a corresponding position, as the retractivity is greatest in these portions. When obstructive atelectasis occurs in the lower and middle lobes, the exudate is situated close to the collapsed parts, as these lobes are retracted and have the greatest capacity of retraction. In the case of obstructive atelectasis of the upper lobe the volume of the upper parts of the lung is decreased and the decrease is compensated for by the expansion of the aereated portions. When an exudate develops these expanded portions of the lung are first reduced to their normal size before they are compressed. The exudate must then first lie under the lower lobe before the latter is compressed. The lower lobe will then float on the exudate and leave more room medially than laterally so that most of the exudate is situated

medially. With an increase in the volume of exudate the lower lobe will become compressed, first along the lateral posterior parts as in normal cases, and the exudate will then also lie laterally and posteriorly.

The author suggests the employment of diagnostic pneumothorax, and roentgenograms with the patient in other positions, to establish the diagnosis of pleural exudate associated with obstructive atelectasis.

J. N. Ané, M.D.

The Frequency of the Finding of Fine Pleural Shadows in the Roentgenograms of Lungs of Children, and Their Dependence on the Roentgenologic Technic. L. Schall and H. Weil. Röntgenpraxis, December, 1934, **6,** 801–803.

The rather frequent finding of fine hair-like shadows, representing parts of the pleura, in children's chest roentgenograms, is dependent on the progress in roentgen technic. Different authors could demonstrate them in different percentages of cases. It seems questionable if any pathologic significance can be attributed to these shadows; in many cases the normal pleura may be shown under ideal conditions of projection and with the best technic. These hair-like shadows were not seen more often in children with a positive tuberculin test than in tuberculin-negative children.

Hans W. Hefke, M.D.

Further Experience with Roentgen Therapy in Malignant Neoplasms of Bronchus and Lungs. G. Herrnheiser. Strahlentherapie, 1935, **52,** 425–459.

In a previous publication the author has urged the use of x-ray deep therapy in malignant tumors of the lungs and bronchi. He analyzes in this article 16 cases of that type treated since 1931; five were still alive at the time of the report. Numerous tables are appended giving the details of the clinical history and particularly all data regarding the treatment technic. While it will be necessary to refer to the original for that information, it may be stated that a total surface dose of 9,000 r is required to bring about regression of this type of tumor. Technic: 170 K.V., 1.2–2.0 mm. Cu, 40 cm. F.S.D., 150–200 cm. sq. field, 1 anterior, 1 posterior and sometimes 1 lateral field, 300–400 r per field per sitting.

Ernst A. Pohle, M.D., Ph.D.

Diagnosis of Congenital Cysts of the Lung. C. de Lange and M. de Bruin. Nederl. tijdschr. v. geneesk., Nov. 10, 1934, **78,** 5127–5136. (Reprinted by permission from Bristish Med. Jour., March 2, 1935, p. 35 of Epitome of Current Medical Literature.)

The authors, who record three illustrative cases, state that until recently congenital cysts of the lung were regarded as a very rare occurrence. During the last few years, however, there has been a great increase in the number of cases published. Sometimes no symptoms are present, so that the condition is found accidentally in the course of physical examination. In most cases, however, there has been some shortness of breath since birth, and the patient has suffered on several occasions from bronchitis or pneumonia. The most important symptom is the occurrence of violent attacks of dyspnea, usually accompanied by cyanosis lasting from a few hours to a few days.

As regards physical signs, multiple small cysts present the appearance of bronchiectasis, while one or more large cysts show the signs of pneumothorax with occasionally considerable displacement of the heart and mediastinum to the healthy side. The diagnosis can usually be made by x-ray examination. The prognosis is probably not so bad as the older writers would lead one to expect.

As regards treatment, the question must be considered as to whether puncture of the cyst is desirable in those cases in which physical and x-ray examination has shown that there is a considerably increased pressure in the cyst. In most cases, however, puncture of the cyst, followed by permanent drainage, is indicated.

An Infected Cystic Lung. Erich Zdansky. Röntgenpraxis, February, 1935, **7,** 79–85.

Multiple cysts of the lung are either congenital or due to bronchiectases acquired in childhood. The roentgenologic appearance is markedly characteristic. The patients suffer often from complicating attacks of bronchitis. Horizontal fluid levels may indicate the presence of secretion. When the lung tissue becomes infected, roentgenograms show areas of infiltration around the cysts, pleuritic thickening, and secondary bronchiectasis. It seems certain that this anomaly is by no means always harmless to the patient.

Hans W. Hefke, M.D.

THE PROSTATE

Prostatic Calculi. L. H. Baretz. Urol. and Cutan. Rev., October, 1934, **38,** 703–706. (Reprinted by permission from British Med. Jour., Jan. 26, 1935, p. 16 of Epitome of Current Medical Literature.)

The author, who records an illustrative case, states that prostatic calculi are not uncommon. According to Kretschmer they are most frequently found in the fifth decade, the youngest in his series being a man of 21 and the oldest one aged 76. Venereal disease plays only a minor part in their causation. Their average number is five to ten and their average size from one-sixteenth to one-eighth inch. They are usually brown or brownish-black in color, and frequently have an iridescent sheen. The outer layers generally consist of calcium phosphate or other earthy salts, such as ammonio-magnesium phosphate and calcium carbonate. Occasionally urates and oxalates are found. The ordinary symptoms are perineal or rectal discomfort, urgency, frequency, and difficulty in micturition. Symptoms of an associated prostatic hypertrophy may be present. Sometimes there are no symptoms at all.

The diagnosis is established by rectal examination and x-rays. In mild cases prostatic massage is indicated, as it may express a small calculus into the urethra. In severe cases operation by the perineal or suprapubic route is required. Baretz's case was that of a man, aged 65, from whom more than 180 prostatic calculi and enlarged prostatic lobes were removed by suprapubic cystotomy.

RADIATION EFFECTS

Blood Disease as a Result of Irradiation. Heinz N. Brinnitzer. Strahlentherapie, 1935, **52,** 699.

The author presents a brief compilation of the various effects of roentgen rays and radio-active substances on the blood, including the blood diseases caused by irradiation. It is arranged under the following headings: Biologic effect of roentgen rays on blood and blood-forming organs in experimental animals and in man, blood changes in professional workers and blood diseases caused by irradiation, blood changes following therapeutic exposures, aggravation of polycythemia following roentgen treatment. A very complete bibliography is appended.

ERNST A. POHLE, M.D., Ph.D.

The Biologic Systemic Effect of Irradiation. R. Reding. Strahlentherapie, 1935, **52,** 545–601.

This is a critical review of the literature dealing with the systemic effect of roentgen rays. Changes in the blood sugar, *p*H, calcium and other minerals, lactic acid, lipoids, nitrogen metabolism, reticulo-endothelial system, the autonomic nerve system, and the blood are considered. While this paper is not suitable for a brief abstract, it is recommended for study in the original because it gives a good conception of the present status of our knowledge. An extensive bibliography is appended.

ERNST A. POHLE, M.D., Ph.D.

RADIUM

Results of Radium Irradiation of Blood Vessels in Circulatory Disturbances. Wilhelm Schloss. Strahlentherapie, 1935, **52,** 652–655.

The author treated 150 patients with circulatory disturbances; 138 were males and 12, females. There were 68 cases of intermittent claudication, 30 cases of endarteritis obliterans, 25 cases of arteriosclerosis, and 27 cases of diabetic gangrene. Superficial radium application was followed by disappearance of the symptoms in 40 cases, while 12 were improved but only temporarily relieved from symptoms; 46 were improved permanently, 12 temporarily, and 40 were not benefited. The hypothesis is advanced that irradiation produces a hormone called "menformon"; it has been shown by Snapper that this hormone improves the circulation in both men and women.

ERNST A. POHLE, M.D., Ph.D.

The Dose Distribution in a Circular Surface Applicator. H. D. Griffith and Karl G. Zimmer. Strahlentherapie, 1935, **52,** 671.

The authors calculated the distribution of radiant energy from a circular radium applicator and compared it with the values obtained by means of an ionization chamber (Sievert condenser type). After certain corrections were made, the two values agreed fairly well. A method is described which permits a homogeneous intensity distribution.

ERNST A. POHLE, M.D., Ph.D.

RESPIRATORY TRACT

Bronchography. A. Beutel. Röntgenpraxis, March, 1935, **7,** 157–167.

The author says that 40 per cent iodipin (Merck) or lipiodol (Lafay) is used for bronchography. If an idiosyncrasy against iodine exists, a bromide-oil mixture may be used. Transglottic injection is the best and simplest method. In more than 500 bronchographies done by the author there has been no complication except occasionally a slight rise in temperature. The trachea may be investigated also by this method. A case of papillomatosis of the trachea is described, the first one to be diagnosed roentgenologically.

Bronchiectases are the most frequent indications for bronchography, and important from a diagnostic standpoint in that bronchiectases which are not visible in flat films may be shown by this method. Exact localization and determination of the extent of the bronchiectases may be found only by this method, when clinical examination, because of hemoptysis, is negative. In other cases the clinical diagnosis may be bronchiectasis, but a bronchography shows no evidence of that disease and the diagnosis must then be putrid bronchitis. Cylindrical bronchiectasis shows the picture of a tree without leaves because there is no alveolar filling. Club-like bronchiectases are much like the saccular type. These are either completely filled or may show a fluid level. Large bronchiectatic cavities may be single or multiple and are often hidden behind liver or heart on flat films. In bronchiectases as in larger cavities, a lipiodol-filling may occasionally not take place when the bronchus is occluded by secretion, blood, etc. A cystic lung has been described by the author.

Bronchography is of comparatively small value for the diagnosis of abscess cavities; plain roentgenograms are usually sufficient.

For the exact localization of fistulas, the injection of contrast material is of great value, but one must remember that non-filling does not mean non-existence of a fistulous tract. Esophageal-bronchial fistulas are usually discovered by giving a barium meal; next in frequency are bronchopleural fistulas.

Extrabronchial expansive processes may compress or displace parts of a bronchus, and bronchograms are occasionally of diagnostic help.

Intrabronchial tumors may show no changes on flat chest films. A bronchogram often allows an easy diagnosis. Several illustrations show the different types of bronchial tumors.

HANS W. HEFKE, M.D.

THE SKIN

Physical Therapy of Cutaneous Epithelioma. Bruno Faccini. Arch. di Radiol., September-October, 1934, **10,** 553–563.

The author regards the presence or absence of metastatic nodes as important as the gross and microscopic characteristics of the lesion in outlining treatment for an epithelioma of the skin. If nodes are present, he favors diathermic coagulation followed at once by roentgen rays; otherwise, diathermy alone can be used. This method of treatment has given satisfactory results over a period of two years.

E. T. LEDDY, M.D.

THE SKULL

Interpretation of Ventriculograms, with Special Reference to Tumors of the Temporal Lobe. A. Torkildsen and A. H. Pirie. Am. Jour. Roentgenol. and Rad. Ther., August, 1934, **32,** 145–153.

In encephalography the authors inject in the third or fourth lumbar interspace, with the patient in a sitting position, and routinely take the following views: anteroposterior, with the brow up; lateral, with the brow up; stereoscopic films with right and left side up; one postero-anterior with occiput up; lateral with occiput up, and anteroposterior with forehead up. One of the two anteroposteriors is given a shorter development, to demonstrate the lighter shadows caused by the anterior horns. The patient's head must be maneuvered so that the gas fills the parts of the ventricles to be shown.

The lateral ventricle is divided arbitrarily into six portions which can be recognized in the antero-posterior view. The lateral view shows the upper outline of the lateral ventricle following the outline of the skull; in a dolichocephalic it is less curved than that of a brachycephalic.

In tumors of the temporal lobe, both lateral ventricles are pushed to the opposite side for a considerable degree. The upper part of the third is likewise displaced, but the lower part remains anchored to the mid-line with a concavity toward the tumor. Dilation of the lateral ventricles and sometimes of the third occurs on the side opposite the neoplasm and compression on the same side. The anterior horn is unaffected. The ventricle of the affected side is lower than its fellow and the roof appears flattened, even concave at times. The descending horn of the affected side is compressed early and, if seen, is pushed upward and toward the opposite side. Very instructive drawings and roentgenograms accompany this paper.

S. M. ATKINS, M.D.

Treatment of Basal Fractures of the Skull. Hesse. Münch. med. Wchnschr., Oct. 19, 1934, **81,** 1605–1608. (Reprinted by permission from British Med. Jour., Feb. 2, 1935, p. 20 of Epitome of Current Medical Literature.)

The author, writing from the standpoint of an otorhinologist, expresses the following views concerning treatment of fractures of the base of the skull. Conservative treatment in the presence of fractures involving the aural, nasal, or accessory nasal cavities is fraught with very considerable risk of a late meningitis, which is almost invariably fatal. Accordingly a special rhinoscopic and otoscopic investigation should be done in the early stage, and x-ray films should be made from the appropriate special angles when fractures of the middle ear, petrous-temporal, or accessory sinuses seem likely. Not all basal fractures are to be detected radiologically, especially those of the roof of the ethmoid, the posterior wall of the frontal sinus, or the roof of the sphenoid. In general, prophylactic operation (exploration and clearing) should be done in comminuted or splinter fractures involving the ear or nasal cavities. In clean-cut fractures near the internal ear expectant treatment is justified except (1) when chronic suppuration of the ear antedates the accident or (2) when the fracture opens into the middle ear. Clean-cut fractures involving the roof or posterior wall of the accessory nasal sinuses justify operation, for intracranial infection is then easier than in fractures affecting the ear. X-ray proof of veiling of the frontal, ethmoidal, or sphenoidal sinuses indicates the possible combination of effusion of blood with small basal fissures; opening of the sinus by draining the hematoma will prevent its suppuration. On the whole, Hesse does not doubt that it is considerably less dangerous in the cases mentioned to open up to the fracture from the temporal zone or from the accessory sinuses than to risk the late onset of serious intracranial complications.

Form, Size, and Position of the Maxillary Sinus at Various Ages Studied by Means of Roentgenograms of the Skull. H. Jobe Sedwick. Am. Jour. Roentgenol. and Rad. Ther., August, 1934, **32,** 154–160.

A detailed study of the size, shape, position, variation, and measurements of the maxillary sinuses at various ages was made roentgenologically. Of the group examined, 80 were triangular, 42, oval; 33, irregular; 9, oblong, and 9, square. The sizes, shapes, and positions varied not only in different individuals but in each side of the same individual. The sinus makes its appearance about the tenth week of fetal life and reaches the maximum size during the third decade of life and does not increase thereafter.

S. M. ATKINS, M.D.

THE STOMACH

The Stomach and Duodenum after Operation. S. Cochrane Shanks. British Med. Jour., Dec. 8, 1934, No. 3857, 1032–1037.

The stomach and duodenum after operation present on roentgen examination many normal variations which must be differentiated from pathologic conditions. The screen examination and the demonstration of the mucosal relief pattern assume even greater importance than in the examination of the intact stomach. Of great assistance is the operative record of the precise type of surgical procedure performed on each case.

The author has divided these post-operative cases from a radiographic point of view into three general classes, as follows: (1) sphincteric control retained, (2) sphincteric control partly retained, (3) sphincteric control abolished. In the group with retention of

sphincteric control the radiographic technic is much the same as in the examination of the intact stomach, except that special attention should be paid to the relief pattern. In some of the cases in which only partial sphincteric control exists and in all of the cases in which sphincteric control is abolished, some method of pressure must be used to occlude the efferent jejunal loop and prevent rapid emptying of the stomach. To accomplish this the author has devised an adjustable truss which consists of a leather-covered spring band, and an adjustable compression pad.

Among the group of cases in which sphincteric control is abolished, the operation most frequently performed and the surgical procedure of choice for simple pyloric obstruction and duodenal ulcer is posterior gastro-jejunostomy. In the erect position the prominent feature of this procedure is the immediate passage of the opaque medium into the jejunum. The pyloric antrum, distal to the stoma, rarely fills to any extent, even if the pylorus has not been occluded in a case of duodenal ulcer. The efferent jejunal loop and the coils of jejunum are usually somewhat distended with barium and a mild permanent dilatation of the upper jejunum is normal. In the supine position a pool in the fundus may remain for a time being there below the level of the stoma. If the stomach before operation was grossly dilated and atonic and its muscle coats too atrophied to be restored to the normal, the radiographic picture after gastro-jejunostomy will be somewhat modified. Some dilatation will remain, the indentations of the greater curvature will be less, and there will be a tendency to pool formation in the pyloric antrum below the stoma.

Because of the incomplete filling of the stomach after posterior gastro-jejunostomy the demonstration of recurrent duodenal, pyloric, or lesser curvature ulcers may be impossible because of the rapid emptying of the stomach. The author's pressure apparatus is especially useful in these cases in permitting all portions of the stomach to fill more completely. In cases in which there is no obstruction of the pyloric canal, the duodenal bulb may be likewise visualized.

The complications of posterior gastro-jejunostomy which may be determined radiographically are as follows: (1) jejunal dumping or "dumping stoma," (2) recurrent lesser curvature, duodenal, gastro-jejunal, or jejunal ulcerations, (3) jejunitis, (4) narrowing of the stoma, (5) malposition of the stoma, (6) duodenal ileus.

The x-ray appearances in anterior gastro-jejunostomy are substantially the same as those in the posterior operation, except that in the lateral view the stoma and jejunal loop are visible anterior to the stomach, and two jejunal limbs, afferent and efferent, are often outlined below the stomach.

Following Billroth II partial gastrectomy the radiographic examination will be similar to that of the gastro-jejunostomies, except that the pyloric antrum will not be visualized. The Polya-Moynihan partial gastrectomy results in a smaller gastric stump than in the Billroth II operation, and the anastomosis will appear to be terminal.

Following complete gastrectomy, radiographic examination shows the meal passing from the esophagus rapidly through the stoma into the coils of the jejunum. Some dilatation of the proximal jejunal loop may be seen, as noted by Butler in a case six months after complete gastrectomy.

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An Analysis of One Thousand Consecutive Examinations of the Stomach and Duodenum from the Clinical, Roentgenologic, and Surgical Viewpoints, with Particular Reference to the Incidence, Diagnosis, and Treatment of Gastric and Duodenal Ulcer and Carcinoma of the Stomach. Nelson M. Percy and David S. Beilin. Am. Jour. Roentgenol. and Rad. Ther., August, 1934, **32** 179–188.

The division of vital statistics at Washington reveals, for 1931, 4,978 deaths from ulcer of the stomach, 2,281 from ulcer of the duodenum, with respective rates of 4.2 and 1.9. From cancer of the stomach, 25,397, or a rate of 21.3. In the authors' 1,000 consecutive cases there were 21 gastric ulcers, 171 duodenal ulcers, and 71 cancers. Of the gastric ulcers, 4.1 per cent of gastric ulcers occurred in the upper third, on the lesser curvature, 20.8 per cent at the middle third, lesser curvature, 12.5 per cent at the lower third on the lesser curvature, and 26.5 per cent at the pylorus. Of the cancers, 8.2 per cent occurred at the upper third, 12.3 per cent at the middle third, and 78 per cent at the lower third. The entire stomach was involved in 1.3 per cent.

All the gastric ulcers had pain: 85.7 per cent in the epigastrium and 14.2 per cent diffuse. Nausea occurred in 52.3 per cent, vomiting in 52.3 per cent, hematemesis in 9.5 per cent, gas in 57.1 per cent, relief from food, soda, or drugs in 28.5 per cent, occult blood in 23.8 per cent, weakness in 38 per cent, anemia in 9.5 per cent, and loss of weight in 42.8 per cent. Duration of symptoms varied from twenty years to four months.

In duodenal ulcers, 92.4 per cent of the patients had pain, of which 75.8 per cent had it in the epigastric and 26.9 per cent in the right upper quadrant. Of the painless cases, 76.4 per cent had hemorrhage and bleeding. Nausea was present in 52.6 per cent, vomiting in 56.1 per cent, gas in 70.1 per cent, while 54.3 per cent were relieved by food, soda, or drugs. Occult blood was present in 46.2 per cent, weakness in 42.5 per cent, loss of weight in 48.6 per cent. The duration of symptoms varied from thirty years to one day. Of these cases, 32 per cent had had previous appendectomies and 18 per cent cholecystectomies.

In gastric cancer, 59 per cent were examined first over six months after the onset of symptoms. The pain was all epigastric. Nausea, vomiting, hematemesis, and gas were greater in the group under 6 months than in those over. For the whole group, the longest duration of symptoms was two years, the shortest three weeks.

The earliest symptoms of carcinoma were vague. When gas, distress in the epigastrium, and nausea are

found in the fifth and sixth decade, a roentgen examination should be made immediately. The absence of free hydrochloric acid is not pathognomonic: 50 per cent of the cases showed free hydrochloric acid in a group reported by Hartment, of the Mayo Clinic. Only 25 per cent of cancers of the stomach are operable when first diagnosed. In a group of 278 cases of the operable type, with no lymphatic involvement, a 5-year cure was obtained by Balfour in 50 per cent.

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SYMPATHETIC NERVOUS SYSTEM

Roentgen Therapy of the Sympathetic Nervous System. Delherm and Beau. Strahlentherapie, 1935, **52,** 629–645.

Exposure of parts of the sympathetic nervous system may be beneficial in a number of diseases. In pruritus ani and vulvæ the local area receives 1 H. per field (80 K.V., 5 mm. Al) until the total dose reaches 1,000 R.[1] The sacral area is exposed in the same manner, with 120 K.V., through 8 mm. Al. In a number of skin diseases, as, for instance, lichen, vitiligo, psoriasis, warts, eczema, keloids, and certain forms of lupus, exposure of the spine (D 4, L 3, and L 4, ganglion stellatum) and the involved area with 500 R through 0.5 Al are recommended. In vasomotor disturbances and Reynaud's disease the authors used a radiation of moderate penetration directed to the cervical and upper dorsal spine for upper extremities and to D 10 to L 5 for the lower extremities. The plexus for each area is also exposed. The filtration varies from 2 to 8 mm. Al and the doses amount to from 400 to 500 R per sitting up to a total dose of from 1,500 to 2,000 R. There is an interval of six weeks between series. In angina pectoris an exposure of the heart and aorta including the ganglion stellatum to irradiation of moderate penetration is often helpful. The dose is from 300 to 500 R per sitting; there are three sittings per week with a total dose of from 3,000 to 5,000 R per field. Hypertension is treated according to the technic of Zimmern and Cottenot by exposing the adrenals. In arteritis obliterans the upper or lower spine is exposed, depending on whether the upper or lower extremities are involved. Technic: 100–180 K.V., 5 mm. Al or 0.25 mm. Zn, one erythema dose per week which may be repeated six times. In a series of 34 cases there were 33.3 per cent cures, 33.3 per cent improvements, and 33.4 per cent failures. In addition to the treatment of the spine, the peripheral plexus is also exposed. In asthma and hay fever good results were observed after exposure of the mediastinum and the spleen: 500 R are given every second day up to a total dose of 3,000 R. In whooping cough, irradiation of the mediastinum may also be beneficial. Well recognized is the use of roentgen rays in the treatment of herpes zoster; both the spine as well as the involved area may be exposed. In syringomyelia and tabes, good results—at least temporarily—may be expected. In a number of endocrine disturbances, roentgen rays can also be of value as a supplementary treatment. In the last part of the article the blood changes seen following irradiation as well as some of the experimental results concerning the effect of roentgen rays on the sympathetic nervous system are briefly recorded.

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[1] Doses expressed in this article are in French R; 2.2 French R correspond to 1 international r.

THE TONSILS

Roentgen Therapy of Tonsillitis. E. D. Dubowyi and I. K. Lusers. Röntgenpraxis, December, 1934, **6,** 815–817.

Fifty patients suffering from tonsillitis have been treated by the authors with roentgen rays (210 K.V., 4 ma., 0.5 mm. Cu, and 2 mm. Al). A skin-focus distance of 25 cm. was used; the field applied just below the angle of the mandible measured 5 × 6 cm.; 100 r were given to each field. The average patient reacted with an increase in temperature and symptoms during the first 24 hours after the treatment. The day following the treatment there was definite improvement, subjectively and objectively. In two cases of a tonsillar phlegmon the improvement was slower and an abscess formed. While patients with a follicular tonsillitis are usually unable to work for from three to six days, the time of disabling sickness is usually cut down to one or two days, exceptionally three to four days, after roentgen treatment.

In 90 per cent of chronic recurrent tonsillitis there was complete and lasting relief from x-ray therapy. Complications due to the treatment with roentgen rays were not noted.

HANS W. HEFKE, M.D.

TUBERCULOSIS, PULMONARY

Intestinal Tuberculosis of the Ulcerating or Cicatrizing Type and its Relationship to Pulmonary Tuberculosis. Giovanni da Empoli. Arch. di Radiol., September-October, 1934, **10,** 481–516.

In the Istituto Diagnostico di Reggio Calabria there have been carried out for some years systematic roentgenologic gastro-intestinal examinations of patients with pulmonary tuberculosis. In this investigation, a high incidence of gastro-intestinal involvement has been found. The author here reports a detailed study made on four such patients and from it he emphasizes the value and importance of roentgenologic examination.

E. T. LEDDY, M.D.

TUMORS (DIAGNOSIS)

Present Status of Diagnosis of Renal Tumors. B. H. Nichols. Am. Jour. Roentgenol. and Rad. Ther., December, 1934, **32,** 769–781. (Reprinted by permission from British Med. Jour., March 2, 1935, p. 37 of Epitome of Current Medical Literature.)

The author reviews various aspects of the radiological diagnosis of renal tumors, and discusses the relative merits of retrograde and excretory urography. The last-named method often reveals characteristic distortion of the pelvis and calices in tumors of the kidney, and provides a fair estimate of the renal function. Further examination by a retrograde pyelogram, if catheterization of the ureter is possible, may give much added information, and should be employed in all cases in which there is any doubt about the diagnosis.

Pneumopyelography has been described as a simple procedure, which causes little or no discomfort, and is unattended by reactions or danger, but Nichols calls attention to the possibility of resultant fatal air embolism. He concludes, however, that, if the catheter is not tightly gripped in the ureter (as occurs in cases of stricture or ureteral calculus), there is little danger of creating a pressure in the kidney that would be at all hazardous, since the air will flow back into the bladder when the pelvis is filled. Radiograms are made while the air is being injected. The author believes that this method has some very distinct advantages in the diagnosis of pelvic tumors or kidney stones.

Pyeloscopy is also of value, especially after the administration of atropine in cases in which the determination of function has already been achieved or is not necessary; it outlines better the deformity of the kidney caused by a renal tumor.

Nichols emphasizes the importance of giving a guarded prognosis, even though the histopathology of a removed tumor is apparently comforting, and points out that a normal radiogram does not eliminate all possibility of the existence of a newgrowth in the kidney.

TUMORS (THERAPY)

Radiation Therapy in Intracranial Tumors. A. Löw-Beer. Strahlentherapie, 1935, **52,** 617–628.

The present status of roentgen therapy in intracranial tumors is briefly discussed. The author uses single doses of from 50 to 120 r. Irradiation is often preceded by spinal puncture to avoid pressure symptoms following treatment. Technic: 180 K.V., from 0.5 to 2 mm. Cu. During the last four and one-half years eight meningeal tumors have been treated, two of which responded well. The author first applied three fields of 605 r each, then changed to the saturation method, and now administers 2,400 r total dose per field over three areas and repeats this after three months. Twenty-eight glioma cases were irradiated and in 16 there was a definite prolongation of life. Three fields are used, 2,700 r was the total dose per field, repeated after three months. Sometimes severe reactions followed a dose of 300 r in one sitting.

Twelve patients having hypophyseal tumors with the symptoms of acromegaly have been treated during the last five years. In six of these the eye symptoms disappeared completely and three showed temporary improvement. From three to four fields are applied, and from 1,500 to 2,500 r are given per area (fractional dose method).

Highly radioresistant are the tumors originating in Rathke's pouch. Four patients of this type were seen. They were treated through four portals with fractional doses of from 1,500 to 3,500 r total dose per field. In only one case was temporary relief obtained.

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